STANDARDS IN CLINICAL DUAL ENERGY X-RAY ABSORPTIOMETRY

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Certificate of Research

This is to certify that, except where specific reference is made, the work presented in this thesis is the result of investigation undertaken by the candidate.

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Declaration.

This is to certify that neither this thesis nor any part of it has been presented or is being currently submitted in candidature for any other degree other than the degree of Doctor of Philosophy at the University of Glamorgan.

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ABSTRACT

Standards in Clinical Digital X-ray Imaging

Dual Energy X-ray Absorptiometry (DXA) is a digital x-ray technique designed to quantify bone mineral density (BMD), primarily of the lumbar spine and hip, and hence to provide a measure of bone strength and propensity to fracture. The original technology was based on a pencil beam x-ray source but later systems use a fan beam. Additional functionality includes measurement of hand BMD and vertebral fracture assessment (VFA). Smaller devices have also been developed to measure BMD at peripheral sites in the body. As the numerical value of BMD resulting from this technique is used directly in diagnosis and decisions over patient clinical management, it is critical that the measurements are accurate and precise.

The work presented in this thesis includes evaluation of the original pencil beam systems, later fan-beam technology, peripheral devices and additional functionality of DXA. This added to the knowledge of the technical capabilities and limitations of the technology providing an indication of precision, factors that may affect accuracy, radiation dose and machine comparison. Novel quality assurance phantoms were designed and constructed for assessing accuracy, precision and long-term stability of DXA-based hand and lateral morphometry techniques.

Research was also conducted into factors associated with BMD, treatment compliance and effectiveness and the role of lateral vertebral assessment. This contributes to the growing body of knowledge on clinical risk factors, medical management and the appropriate use of DXA and VFA.

The thesis also includes the author's contribution to the national training scheme and development of guidelines which have helped raise standards of the technique nationally.

These three areas of work contribute to ensuring the safe use of the new and developing technology and appropriate application within the clinical environment supported by highly trained operators and guidelines.

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Glossary of Terms

Accuracy In the context of DXA accuracy is the agreement between measured (i.e. biased) BMD and true BMD. A measure of ashed weight of bone is the gold standard.

BMD Bone Mineral Density measured using DXA. This is an areal measurement of bone mineral content per unit area:

$$BMD = \frac{BMC(g)}{\text{Bone Area } (cm^2)}$$

DXA Dual Energy X-ray Absorptiometry

HRT Hormone Replacement Therapy is a therapeutic treatment used in women to replace hormones that the body no longer produces following the menopause. The hormones are oestrogen and progesterone.

IRMER The Ionising Radiation (Medical Exposure) Regulations 2000 is a statutory instrument designed to protect patients and research subjects from unnecessary radiation exposure. In November 2006 enforcement of the regulations was transferred from the Department of Health to the Healthcare Commission.

LVA Lateral Vertebral Assessment is the terminology used by GE-Lunar for the measurement of vertebral height by DXA on their equipment.

MXA Morphometric X-ray Absoptiometry which is a DXA technique for measurement of vertebral height. This later became known as Lateral Vertebral Assessment (**LVA**) and current nomenclature is Vertebral Fracture Assessment (**VFA**) which is a generic term for all technologies.

NOS The National Osteoporosis Society is a charity established in the United Kingdom in 1986. The charity is dedicated to improving the diagnosis, prevention and treatment of osteoporosis.

Precision A measure of reproducibility ie. degree of agreement of repeated measures. Determined by the root mean square coefficient of variation (rmsCV%).

Sensitivity In the context of peripheral DXA is the ability of the measurement to identify those with the disease (in this case osteoporosis as defined by a T-score of below -2.5 at spine or hip by DXA).
Sensitivity is True positives identified as a proportion of all those with osteoporosis.

Specificity In the context of peripheral DXA is the ability of the measurement to identify those without osteoporosis as defined by spine or hip DXA.

Specificity is True negatives as a proportion of all those without osteoporosis.

T-score Describes BMD relative to a young normal population in terms of number of standard deviations from the young normal mean BMD:

$$\text{T-score} = \frac{\text{Measured BMD - Young Normal Mean BMD}}{\text{Standard Deviation of Young Normal Population}}$$

VFA Vertebral Facture Assessment is the determination of vertebral morphometry using medical imaging techniques to diagnose vertebral fracture. The techniques include lateral spine DXA and standard x-rays.

Z-score Describes BMD relative to a normal population of the same age in terms of number of standard deviation from the age-matched mean BMD:

$$\text{Z-score} = \frac{\text{Measured BMD – Age-Matched Mean BMD}}{\text{Standard Deviation of Age-Matched Population}}$$

CHAPTER I

INTRODUCTION

1.1 Problem Outline

The introduction of Dual Energy X-ray Absorptiometry (DXA) in the late 1980s provided a practical diagnostic tool for prediction of propensity to fragility fracture. Unlike other clinical diagnostic technologies such as standard radiography (x-ray), Computed Tomography (CT) and Magnetic Resonance Imaging (MRI), DXA had only one application, the measurement of bone mineral density (BMD). DXA also appeared to be a relatively simple technique which provided a quantitative measure of bone strength that could be compared with a normal reference range. Hence the technique was primarily adopted by clinicians whose patient group included those at risk of osteoporosis and fragility fracture. With the introduction of a definition for osteoporosis based on a measure of BMD by DXA and the development of more bone protective drugs, there was increasing interest in the use of DXA.

At the time there was little independent evaluation of the equipment and a lack of training, procedures and guidelines to ensure optimisation of the results achieved. As a minor change in BMD is associated with a major change in fracture risk, equipment quality assurance and adherence to good operating technique is paramount. However, few DXA systems were placed within a scientific and technological healthcare environment that could adequately address these requirements.

At the author's unit in Hull, where most of the research presented in this thesis was carried out, the first DXA system to be installed was placed within the Nuclear Medicine Department which is part of the Medical Physics Service. This provided the appropriate environment, equipment and skilled staff to conduct the independent assessments necessary for equipment evaluation and validation. Being a new technology within the clinical field, protocols and standard operating procedures were required, and policies and guidance on appropriate clinical application.

1.2 Aim

The work presented within this thesis was conducted with the aim of ensuring safe use of this new and developing technology and appropriate application within the clinical environment supported by highly trained operators and guidelines.

This aim was achieved by research into the following three aspects of DXA technology and its application.

1.2.1 Equipment

The work presented in this thesis includes commissioning and acceptance testing, radiation protection assessments, in-vitro and in-vivo precision, resolution and evaluation of new functionality of various types of DXA units from the original pencil beam systems through fan-beam rotating C-arm to semi-fan beam and peripheral units. Bespoke test equipment to confirm equipment accuracy and precision was designed and constructed and these devices remain in weekly use for the monitoring of scanner performance and precision.

1.2.2 Clinical Application

Also presented is research into the clinical application of DXA including an assessment of the technical and logistical feasibility of population screening, investigation of risk factors for osteoporosis and use of DXA based vertebral morphometry.

1.2.3 Standards

Finally, the author's contribution to national guidelines and a training scheme for DXA operators is detailed. These were developed with the aim of raising the understanding, quality and standards of the technique nationally.

1.3 Contribution to Knowledge

The work performed by the author over the years has added significantly to the growing body of knowledge on the performance, limitations and utility of the DXA technique and evolving technology. This thesis claims the following

contribution to knowledge in the three areas outlined above:

1.3.1 Equipment

1.3.1.1 The comparison of 4 DXA systems from the same manufacturer (section 2.3) was one of the first to indicate the importance of ensuring patient follow-up on the same machine, a recommendation that is still relevant today. This work also demonstrated the inherent errors associated with soft tissue inhomogeneities that may affect accuracy of BMD particularly in the elderly.

1.3.1.2 The radiation assessment of the Lunar Expert-XL (section 2.4) was the first to be performed on the new generation of higher resolution DXA systems. The findings confirmed the increased radiation burden to patients and staff. As a result this device was subsequently discontinued as users favoured alternative, lower dose systems in order to comply with the need to keep radiation doses as low as reasonably achievable.

1.3.1.3 Two phantoms were designed and constructed that were the first available for use in evaluation and quality assurance of bone mineral density of the hand and morphometry of the spine using DXA equipment (section 2.6). These proved to be of significant interest particularly to University based DXA units and have been used by sites in the UK and Europe.

1.3.1.4 The initial research work with the hand phantom demonstrated that the original pencil beams proved inadequate for performing in-vivo bone densitometry of the hand (section 2.6.1), a procedure which rheumatologists at the time were interested in for the management of patients with rheumatoid disease. The Expert-XL was later found to be more suitable for this application.

1.3.1.5 Evaluation of a new heel DXA device incorporating a laser measure of heel thickness demonstrated that this gives improved precision over a standard DXA heel device. There were no diagnostic thresholds in existence at the time so these were established and incorporated in national guidance on clinical use of the device (section 2.7.2).

1.3.1.6 The evaluation of an x-ray based technique for measuring only hand bone density provides an indication of precision and appropriate thresholds for use as a clinical triage tool (section 2.7.3).

1.3.2 Clinical Application

The work presented in this thesis has also contributed to an improved understanding of the clinical role of DXA.

1.3.2.1 A paper on the technical and logistical feasibility of population screening was a seminal paper which demonstrated the robustness of the equipment and acceptability of the technique although such screening is not currently supported on cost effectiveness grounds.

1.3.2.2 A study of patients with coeliac disease confirmed an adverse effect of this condition on BMD even after matching for height, weight, menopausal status and menopausal age (section 3.4.3). The presence of coeliac disease was therefore included in the local referral criteria for DXA.

1.3.2.3 Papers on the adherence to (section 3.5.1) and the bone protective effects of (section 3.5.2) hormone replacement therapy provided insight into patient acceptability of HRT in a normal clinical setting and subsequent effect on bone of a short course of therapy. The latter was particularly relevant following the adverse publicity around the side effects of HRT and concerns over the reported increased cancer and heart disease risks associated with long term medication.

1.3.2.4 A comparison of targeted versus routine use of lateral imaging of the spine by DXA for diagnosis of vertebral fractures included the largest reported cohort of patients at the time to undergo the technique (section 3.6). This has proved of interest to those looking at the potential of introducing this into their clinical practice and will help groups involved in developing guidance on the use of DXA based spine morphometry.

1.3.3 Standards

1.3.3.1 A training scheme was developed which was the first national scheme for certification of bone densitometry operators (section 4.3). Contributions towards its design, literature, teaching materials and marking scheme are presented. The scheme has been attended to date by 589 students with 264 proceeding to full certification. The scheme is endorsed by the College of Radiographers and the Institute of Physics in Engineering and Medicine and recognised by the Royal College of Physicians. Evidence of successful completion of this scheme is now

included by some employers in the person specification for applicants to bone densitometry vacancies.

1.3.3.2 Guidelines on the setting up of a DXA based bone densitometry service were the first available nationally to aid commissioners, service providers and practitioners and also provide a benchmark for auditing of existing services (section 4.4.1).

1.3.3.3 Guidance on interpretation of DXA results was the first available in the UK to help practitioners involved in the scientific and clinical interpretation of DXA scans and provision of a report to the referring clinician (section 4.4.2).

1.4 Thesis Structure

The following three chapters take each of the areas of work in turn: equipment, clinical application and standards, identifying the gaps in knowledge at the time, explaining the motivation for the activities and how the results contribute to the understanding and appropriate application of the DXA technique. The thesis structure is outlined in Figure 1.1.

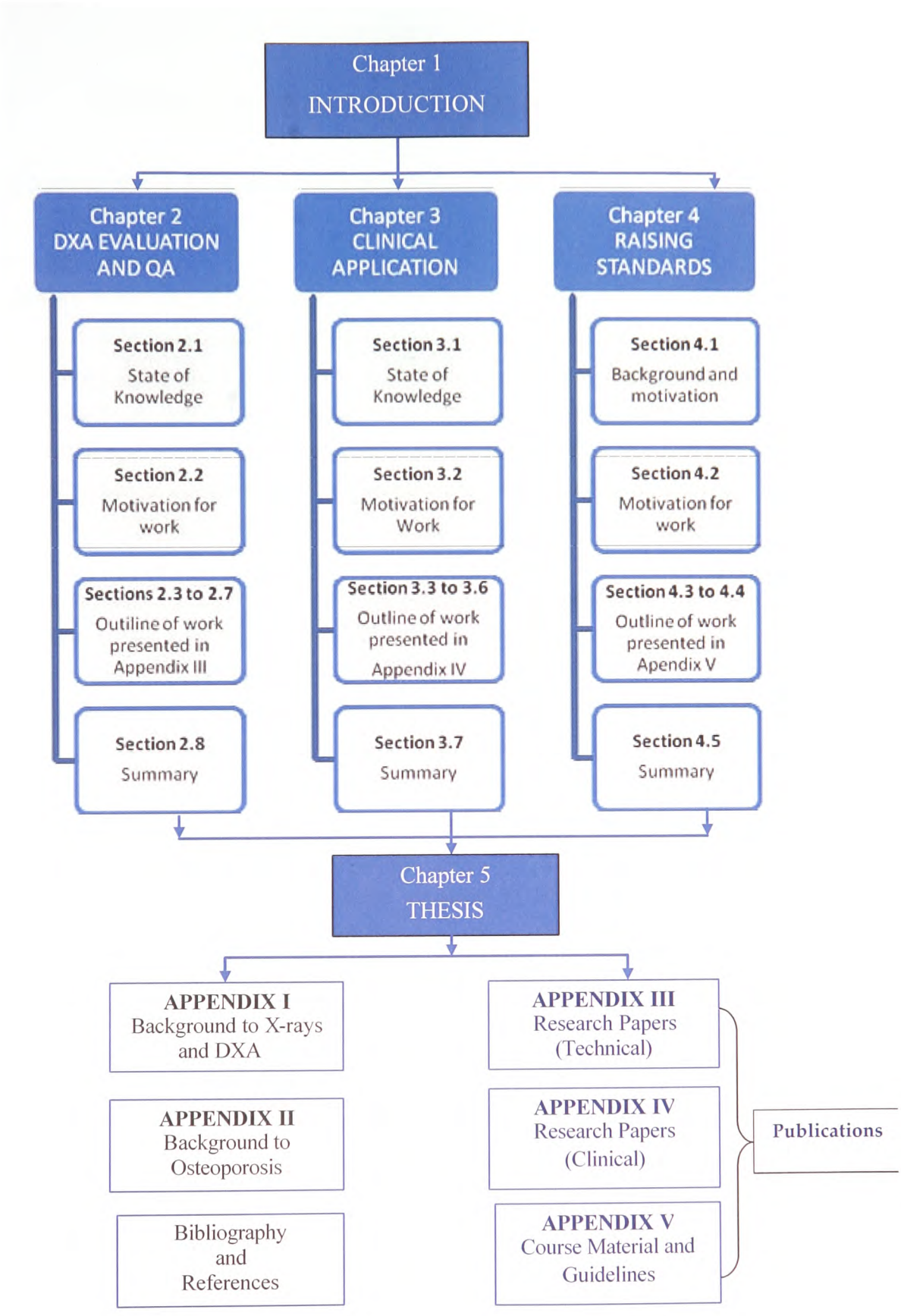


Figure 1.1 Diagram of Thesis Structure

CHAPTER 2

EQUIPMENT EVALUATION AND QUALITY ASSURANCE

2.1 Outline of the State of Knowledge at the Time

2.1.1 Introduction

The work presented in this thesis is based on the evaluation and clinical application of DXA which was designed to quantify bone mineral density, primarily of the lumbar spine and hip, and hence provide a measure of bone strength and propensity to fracture[1 2 3]. The technique is based on the attenuation of two different energy x-rays by the body. Background information on the production and attenuation of x-rays and the development of DXA is provided in Appendix I. By selecting two x-ray photon energies of around 40 and 80 keV, it is possible to differentiate between the attenuation due to bone and soft tissue. On passing through the human body, the low energy x-rays are attenuated more than the high energy, but especially so by bone. The transmitted x-ray signals are digitally stored on personal computers (PCs) containing dedicated software packages for image display and analysis. The system is calibrated to give an areal bone mineral density (BMD) in gcm^{-2} using bone and tissue standards of known density. As the numerical value of BMD resulting from this technique is used directly in diagnosis and decisions over patient clinical management, it is critical that the measurements are accurate. Patients may be followed up with repeat DXA measurements to monitor changes in BMD due to disease progression or treatment-related changes with minor changes in BMD reflecting major changes in fracture risk. Consequently, the DXA systems must be capable of providing a precise measure of BMD both short- and long-term.

With the introduction in 1994 of the WHO definition for osteoporosis based on a measurement of BMD by DXA (Appendix II 1.3) the status of reduced bone mineral density and susceptibility to fracture following minimal trauma became identifiable as a disease status even in the absence of an existing fracture. This opened up possibilities of screening patients, identifying those at high risk, and prescribing bone protective treatments in an attempt to prevent fractures. There was a consequent rapid deployment of DXA equipment with no guidance or controls over operation or usage. There were and remain two major manufacturers involved, both U.S. based, who enforced customer brand loyalty

through lack of agreement on software algorithms for determination of BMD and inconsistencies of reference databases. Device specific dedicated software was developed and reference databases established for comparison. This was a new and fast developing quantitative digital imaging technique in medicine where relatively small changes in the parameter being quantified (BMD) became clinically very significant[4].

2.1.2 DPXL

The early DXA devices used a pencil beam of x-rays and a sodium iodide scintillation detector. The two were mounted onto a C-arm and moved in unison in a rectilinear fashion over the area of interest. One such system was the Lunar DPX (GE-Lunar, Madison, Wisc.) illustrated in figure 2.1.

Figure 2.1 Lunar DPX bone densitometer

These machines had an x-ray tube operating at 80kV and used energy-selective filtration via a Cerium k-edge filter to achieve the spectral characteristics required. Scans could be performed of the lumbar spine and hip up to 167 lines, 1.2 mm apart consisting of 1.2 mm spaced sample points. Total body scans of 205 lines were possible and the DPXL version enabled lateral scans of the lumbar spine. Different scan speeds were provided to accommodate varying tissue thicknesses. Medium speed was generally used giving a scan time of 4 minutes and skin entrance radiation dose of less than 15 μSv. For patients less than 22 cm thick within the scan area, fast scan mode could be used with a scan time of about 1 minute and radiation dose of 5 μSv. For larger patients, over 26

cm thick, slow mode was recommended to compensate for reduced counting statistics due to increased attenuation. Scan times were increased to 8 minutes and doses to about 30 μSv.

In the early days following the introduction of DXA there was little independent equipment evaluation in particular regarding inter-machine variability and the effect of physiological variations in tissue thickness or composition. The concept of Dual Energy X-ray to differentiate between the attenuation through the two main components of the volume being scanned assumes that soft tissue is of a constant composition across the region of interest. However, soft tissue is composed of lean tissue (muscle) and fat tissue in varying proportions between individuals and, probably more critically, the proportion of red (lean) and yellow (fatty) bone marrow differs with age. Another anatomical variant which could affect accuracy of DXA is thickness of the body in the region being scanned. This can lead to beam hardening or detector saturation as described in Appendix I (2.9) and to area measurement errors due to the changed position of the bone relative to x-ray source and detector. In the early days of DXA there was a need for independent evaluation of these patient-related potential artefacts. Also, as there was a possibility of longitudinal monitoring of BMD changes, advice was required on whether follow-up scans could be performed on any scanner from the same manufacturer.

There was limited knowledge at the time of short and long term precision which could inform the user of the ability of DXA to measure and monitor changes in bone mineral density to the degree of accuracy and precision required.

2.1.3 Expert- XL

The Lunar Expert-XL, one of the first fan beam DXA systems, provides faster, higher resolution images but at an increased radiation dose (Figure 2.2). The Expert-XL uses a fan beam of x-rays and an array of solid state scintillation detectors, the x-ray tube and detectors being mounted on a C-arm which may be rotated to enable both anteroposterior and lateral imaging. The detector array eliminates the need for the rectilinear scanning motion required with traditional pencil beam systems, the emitter/detector assembly moving only longitudinally. The x-ray tube operates at a voltage of 134 kV and maximum tube current of 5 mA with 2 mm aluminium filtration. Dual energy discrimination is achieved at the

detector by one row of elements recording the low-energy and one the higher-energy x-rays. The system is capable of performing bone densitometry assessment of the lumbar spine, femoral neck, whole body, forearm, hand and morphometric assessment of the thoracic and lumbar vertebrae.

Figure 2.2 Lunar Expert-XL bone densitometer

Fan beam DXA systems involve an increased radiation burden for both patient and staff compared to the original pencil beam systems.

> **Njeh *et al.*[5] examined the doses involved for a prototype Expert DXA system but there was no independent assessment of the Expert-XL.**

Digital imaging produces a course representation of bone edges resulting in some pixels containing both bone and soft tissue. This can introduce errors in edge detection and hence in measured bone area which in turn affects BMD. The improved resolution and faster scan speeds of the Expert-XL potentially offered improved precision through reduction in edge detection errors and motion artefacts. The almost radiographic quality images opened up the possibility of deriving morphometric parameters particularly of the vertebral bodies. The proprietary literature states a range of maximal resolutions from 2 to

1.6 line pairs(lps)/mm (0.5 mm to 0.625 mm) and others reported resolution of 0.95 to 0.7 lps/mm (1.05 to 1.43 mm) for the prototype Expert [6].

However, there was no independent assessment of image resolution of the Expert-XL to indicate the degree of accuracy of this procedure.

2.1.4 Prodigy

In 2001 the Lunar Prodigy narrow fan beam system (Figure 2.3) was introduced which offered improved resolution but at a lower radiation dose than the Expert-XL. The Prodigy utilises a narrow fan beam in the cranio-caudal direction which performs a raster-type scan across the area of interest. The x-ray tube, which is mounted below the table, operates at a constant potential of 80 kV and uses a k-edge filter (Cerium) to provide 2 energies of around 40 and 70 keV (Appendix I:2.2).

However, there was no independent report on the Prodigy densitometer and no indication of how well the results agreed with the DPX systems which they were often replacing.

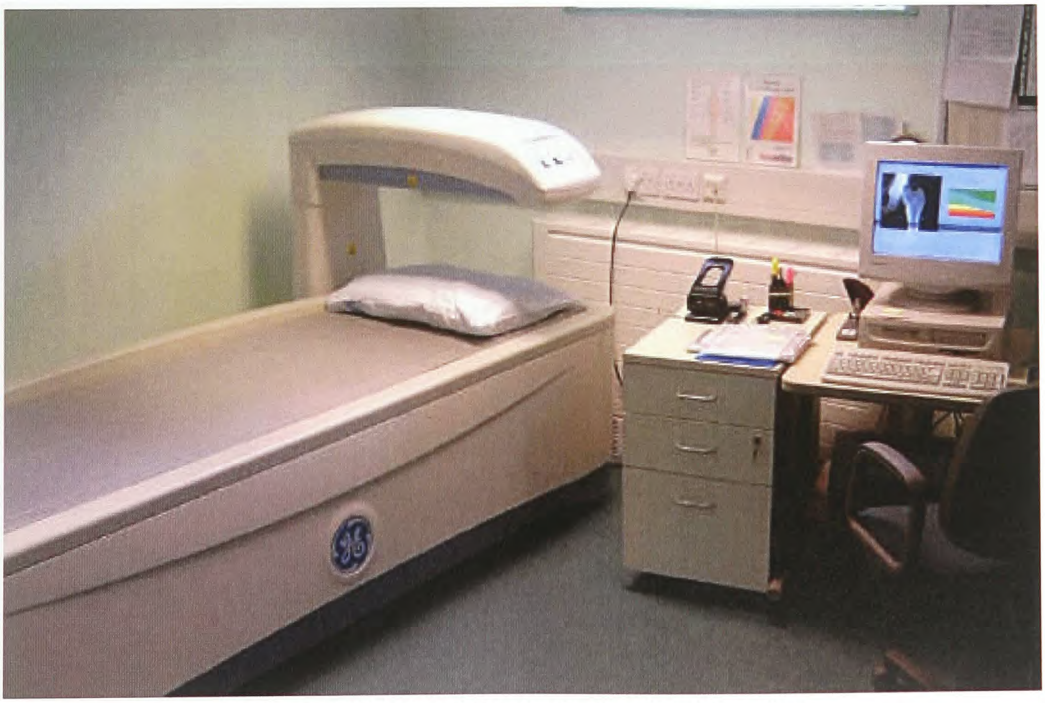


Figure 2.3 Lunar Prodigy bone densitometer

2.1.5 Quality Assurance Devices

DXA hardware and software developments continued through the 1990's with the introduction of additional functionality.

2.1.5.1 Hand DXA

Development of DXA software during the 1990s included the introduction of protocols for hand bone density on the Lunar DPX which was seized by some rheumatologists as a means of staging and monitoring rheumatoid disease by examining changes in peri-articular BMD of the hand.

Hand acquisition and analysis software was also made available for the later introduced Expert-XL (Figure 2.4).

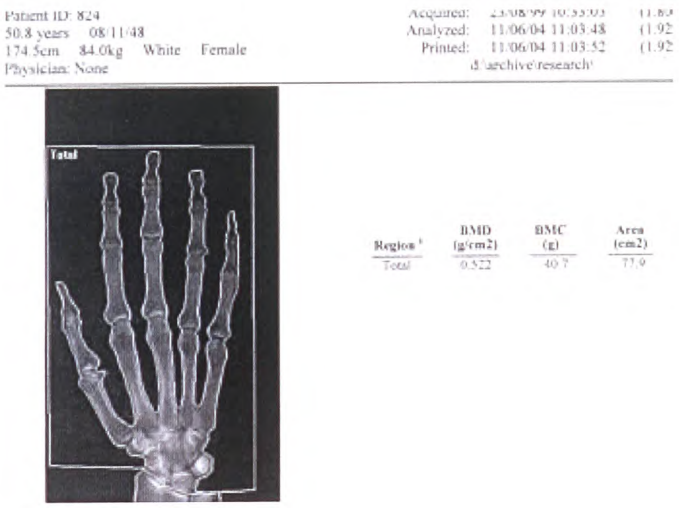


Figure 2.4 Hand scan performed on a Lunar Expert-XL showing a measurement of hand BMD

In 1994 Peel *et al.* studied 70 postmenopausal women with established rheumatoid arthritis on a Hologic 1000 and compared them to 20 controls and 20 early RA cases. They concluded that the technique was accurate and precise and could provide a marker for disease progression[7].

However, no quality assurance device existed that was suitable for the smaller tissue volumes and lower bone density seen in the hand.

2.1.5.2 MXA

With the advent of the Expert-XL fan beam DXA system, measurement of vertebral deformity by lateral imaging became possible. The improved resolution also facilitated accurate identification of vertebral endplates in order to determine deformities from a change in anterior, mid and posterior heights. Morphometric x-ray absorptiometry (MXA) provided the potential for identifying undiagnosed vertebral fractures at the same time as obtaining the diagnostic spine and hip BMD without the need for additional, higher radiation dose radiographic procedures. This became important in clinical management of the patient as emerging evidence identified prior fragility fracture as a major risk factor for future fracture[8 9 10] although fragility fractures of the spine often go undetected and unreported[11].

The technique lacked a quality assurance tool for use in in-vitro validation, stability and precision. Also, there was no information on the effect of kyphosis and scoliosis, features common in the patient population studied with this technique.

2.1.6 Peripheral DXA Devices

Many regions in the UK still do not have access to DXA services locally and cannot obtain the financial support to establish a service. As a newly 'discovered' disease, osteoporosis does not figure highly alongside the long established and high profile diseases such as cancer, heart disease and diabetes. Also, diagnosis and management of a pre-morbid, symptom free condition may be considered more suitable for management within primary care and not requiring the specialist services of secondary care.

With the change in NHS financing introduced in the 1990's, the newly established Primary Care Trusts (PCTs) became the NHS fund-holders, purchasers and commissioners of healthcare. The PCTs were obliged to allocate a proportion of their budget to nominated key disease areas through the

Local Delivery Plans with secondary care services, but the remainder was increasingly being invested in establishment of services within Primary Care. Equipment manufacturers quickly recognised the potential of smaller, cheaper, portable devices that could measure bone density and prove more suitable for placement in a Primary Care setting.

2.1.6.1 PIXI

The PIXI (Ge-Lunar Corp) peripheral densitometer was introduced in 1998 (Figure 2.5). This uses a cone beam x-ray source of 80kVp and tube current 400μA. The x-rays are filtered using a polycarbonate and brass/zinc/copper composite filter to produce 2 peaks of 55keV and 80keV. There are no moving parts during acquisition.

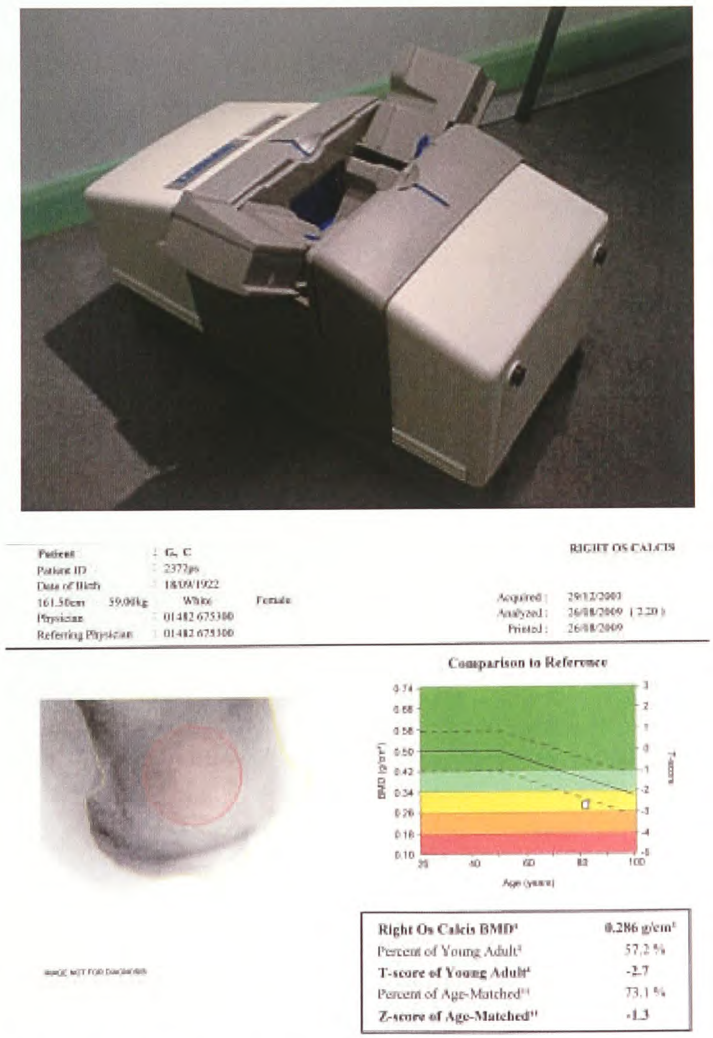


Figure 2.5 The PIXI peripheral bone densitometer (GE-Lunar, Madison Wisc). In configuration for heel BMD (above) and results printout (below).

The device is designed to be floor standing for measurement of calcaneal BMD (see Figure 2.5) or inverted and placed on a bench top for measurement of forearm BMD. The PIXI was marketed as a simple, portable device that could be utilised in Primary Care.

However, there was no independent guidance on appropriate application of this technique or on interpretation of the results in terms of patient management.

2.1.6.2 Calscan

A new peripheral device for calcaneal BMD using fan beam configuration DXA was introduced in 2000. The DXL Calscan (Demetech AB, Sweden etc.) also incorporates a laser measurement of heel thickness in an attempt to improve the accuracy of calcaneal BMD (Figure 2.6). The heel thickness is used to correct inaccuracies introduced by the assumption in normal DXA systems that there is a homogeneous distribution of lean and adipose tissue within soft tissue[12 13]. Attempts at utilising 3 x-ray energies to overcome the problem of inhomogeneous soft tissue was suboptimal due to increased scan times and radiation dose[14 15].The measurement of heel width was found to provide the third component needed[16].

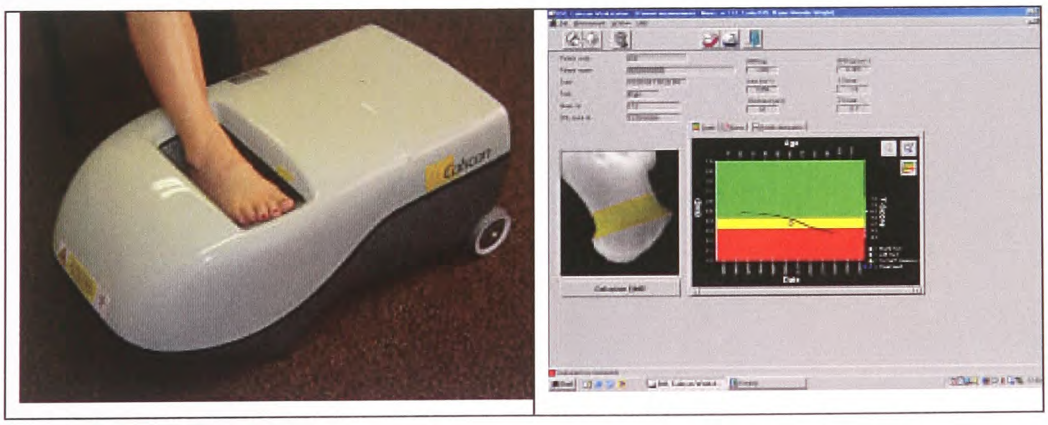


Figure 2.6 The DXL Calscan heel DXA device and results display.

There was no independent evaluation of this device or comparison with other standard heel DXA devices.

2.1.6.3 Metriscan

Peripheral devices are also available for quantifying bone mineral density of the hand. The Metriscan is a compact digital radiographic absorptiometry device capable of measuring bone mineral content of the second phalanges of the middle three digits (Alara Incorporated, Hayward, California, USA) (Figure 2.7). The device uses a cone beam x-ray (tube voltage 60 kV, current 0.333 mA) and the image is projected onto a curved storage phosphor plate mounted on a rotating drum. The drum is rotated, and scanned by laser, to excite photons from the surface of the exposed phosphor plate, with a photosensitive detector converting these photons to an electronic signal pulse proportional to the number of incident photons. A second light source then erases the plate ready for the next acquisition. An aluminium step wedge of known thickness built into the device within the region of interest provides calibration for each image. Bone mass estimates are determined through comparison with the step-wedge, and T- and Z- scores are derived from reference data. Results are expressed as BMD, but as there is no comparison against a known bone-standard, the BMD score given is an arbitrary unit (BMD_{au}), rather than the usual gcm^{-2}. Although not a DXA device, this was marketed similarly to the peripheral DXA systems and is included for completeness.

At the time there was little independent evaluation of this technique and no advice on interpretation of the results for patient management.

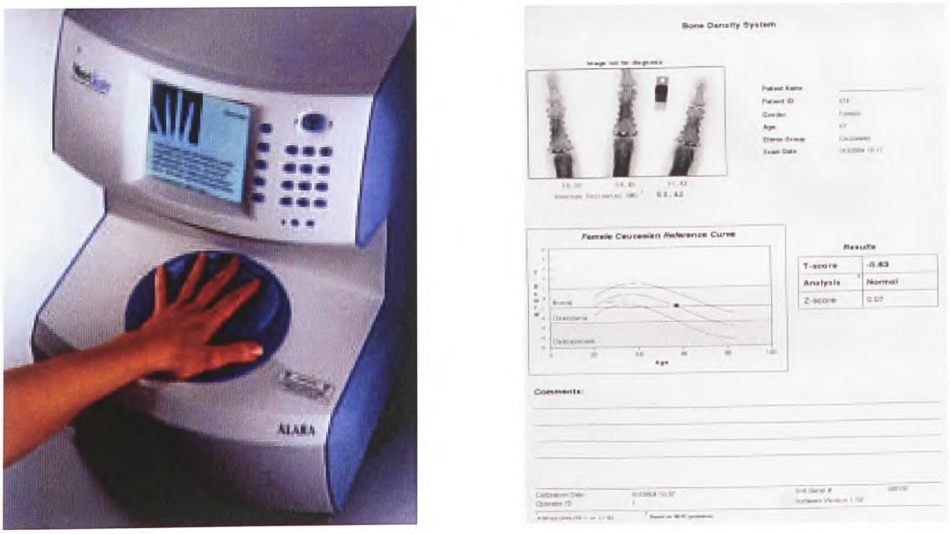


Figure 2.7 The Metriscan digital radiographic absorptiometer

2.2 Outline of the Motivation and Significance of the Work Undertaken

The motivation for the work presented in Appendix III was to contribute to the understanding of factors associated with the measurement of bone mineral density and additional DXA functionality. This knowledge was used locally to inform policies and procedures governing the use of the technology within a routine clinical environment. Also, through publications and presentations, the work contributed to the growing body of knowledge on the subject. The areas to be investigated evolved over the years with the development of improved technology, additional functionality and introduction of new devices.

The following objectives were set to address the shortcomings raised above in this chapter.

2.2.1 Objective 1 was to evaluate the DPXL pencil beam densitometers, assessing accuracy, precision, effect of tissue depth and composition on BMD and the inter-machine variability. This helped to determine equipment and patient related factors which could influence the measurement of BMD.
This objective is addressed in Section 2.3.

2.2.2 Objective 2 was to evaluate the later introduced Expert-XL fan beam densitometer, determining radiation dose, precision and resolution. This helped inform decision on the appropriate use of this improved resolution but higher radiation does device.
This objective is addressed in Section 2.4.

2.2.3 Objective 3 was to assess the precision and radiation dose of the Prodigy densitometers and examine the relationship between BMD determined using this device compared to the DPXL.
This objective is addressed in Section 2.5.

2.2.4 Objective 4 was to design a phantom for quality assurance of hand BMD by DXA. No such phantom existed at the time to assess the accuracy and precision of this new DXA development.
This objective is addressed in Section 2.6.1.

2.2.5 Objective 5 was to design a phantom for quality assurance of Morphometric X-ray Absorptiometry (MXA) and use this to determine affect of patient positioning on vertebral height measurement. Again, there was no phantom at the time to determine and monitor accuracy and precision of this new technique.
This objective is addressed in Section 2.6.2.

2.2.6. Objective 6 was to evaluate the PIXI peripheral DXA system and examine the relationship between heel BMD and axial BMD. This was to determine the reliability of these measurements and whether they were related to BMD measured by standard hip and spine DXA in order to inform decisions on appropriate use.
This objective is addressed in Section 2.7.1.

2.2.7. Objective 7 – to evaluate the DXL Calscan heel densitometer and derive triage thresholds for clinical use. As above, this helped development of operating protocols and provided guidance for users on patient management based on the BMD result.
This objective is addressed in Section 2.7.2.

2.2.8. Objective 8 – to evaluate the Metriscan hand densitometer and derive triage threshold for clinical use. Again, this helped with consideration of appropriate placement of this technology in the clinical arena and provided patient management guidance based on the result.
This objective is addressed in Section 2.7.3.

2.3 Objective 1: Evaluation of Lunar DPX Bone Densitometers

2.3.1 Inter-machine Variability and Accuracy

The equipment evaluation presented in this chapter stems from a thorough understanding of the DPX technology gleaned whilst undertaking a project as part of an MSc. This is presented here as it establishes the basis of the techniques used for assessment of later technologies. Work was carried out to

determine the difference in measurement of BMD between 4 Lunar DPX machines and the effect of anatomical variants that may affect this measurement. Repeat scans were performed of an aluminium spine phantom on 4 Lunar DPX pencil beam DXA systems. The results demonstrated that although phantom BMD was within ± 2% of the manufacturer's stated value on all systems, there was a small but significant variation between the machines.

The recommendation was made that if repeat scans are required to monitor change, they should be performed where possible on the same scanner.

DXA theory assumes that the body is composed of only two components, bone and soft tissue. However, soft tissue is composed of lean and fat tissue which have slightly different attenuation properties at the energies used in DXA. There are variations in fat content of soft tissues between individuals and within individuals over time. This should be compensated for by the software as the k value (or R value on Lunar systems) is determined at the time of scanning. This value is derived from the ratio of attenuation of the high and low energy x-rays through the soft tissue area. Investigations using a soft tissue substitute of varying fat composition confirmed that BMD was not significantly affected by changes in fat to lean composition that would be encountered in clinical practice.

The software compensation for variable soft tissue composition described in the previous paragraph assumes that the soft tissue composition within the path of the x-ray beam over the bone area is the same as that adjacent to the bone. This may not always be the case especially with increasing age and replacement of red bone marrow with more yellow (fatty) marrow. Using varying thicknesses of a fat equivalent material to displace the water overlying the phantom only, leaving the adjacent 'soft tissue' areas constant, there was found to be a highly significant drop in BMD of 4.3% per cm of excess fat in the bone area. This is due to the correction for soft tissue being based on the differential attenuation in the areas adjacent to bone. In clinical practice, the fat content between the bone region and adjacent soft tissue may vary from -2.7 to 18.7% [17] hence this may have a significant effect on measurement of BMD. Others later demonstrated errors of around 5%[18] although a cadaver study suggested the errors were within acceptable limits[19].

The position of the spine may vary relative to the bed due to increased soft tissue thickness or spinal curvature which may affect estimate of BMD by DXA. Using a stepped holder for the spine phantom purpose designed by the author, a significant decrease in BMD with increasing height of the phantom was demonstrated on two of the four DPX pencil beam systems.

The effect of variations in soft tissue thickness within the scan area on measured BMD was also investigated. It is possible that in obese patients beam hardening due to selective attenuation of the low energy x-ray component can artificially raise measured BMD. Alternatively, in very thin individuals there will be reduced attenuation of the x-rays leading perhaps to detector saturation. The DXA software provides different scan modes which vary the photon flux and scan speed to accommodate these variations but there was a lack of independent validation. It was found that use of appropriate scan mode minimised potential overestimate of BMD in cases of increased tissue thickness.

This work provided insight into the factors affecting measurement of BMD using a pencil beam densitometer and the potential of the equipment for monitoring longitudinal changes in BMD. This contributed to the design of further research activity presented below involving the newer technology fan-beam and semi-fan-beam densitometers (sections 2.4 and 2.5) and peripheral densitometers (section 2.7).

2.3.2 Long Term Precision of DPXL

A meta analysis by Marshall *et al.* reported that a reduction in BMD equivalent to one standard deviation (equivalent to approximately 10% change in BMD) of the reference population is associated with an approximate doubling of risk of fragility fracture [4]. Consequently, the DXA systems must be capable of providing a precise measure of BMD both short- and long-term. A rigorous quality assurance procedure was introduced by the author which involved daily scanning of spine phantoms on each of three DXA systems and scanning of one phantom on all three systems for cross calibration purposes. This enabled a detailed analysis of equipment stability and effect of component failure and replacement (Abstract 1). Over a seven year period, the systems were found to be robust with good long-term in-vitro precision of 0.8% (Table 2.1).

Machine	Phantom number (reference BMD)	Number of scans	mean (SD) BMD L2-L4 (gcm^{-2})	precision (CV %)
DPXL (1)	2115 (1.282 +/- 2%)	1060	1.263 (0.010)	0.81
DPXL (2)	1583 (1.267 +/- 2%)	1315	1.267 (0.010)	0.82
DPX	1275 (1.283 +/- 2%)	1384	1.277 (0.010)	0.78

Table 2.1 Long term (7 year) precision of 3 DPX(L) scanners

The three systems were found to give similar BMD results for the cross-calibration phantom (Table 2.2).

Machine	Number of scans	Mean (SD) BMD L2-L4 (gcm^{-2})	precision (CV %)	difference
DPXL (1)	313	1.274 (0.009)	0.70	+ 0.5 %
DPXL (2)	1395	1.267 (0.010)	0.82	0 (ref.)
DPX	1384	1.258 (0.010)	0.79	- 0.7 %

Table 2.2 Correlation between machines using same phantom (reference BMD 1.267 gcm^{-2})

Detector deterioration on all systems caused a decline in spine phantom BMD of about 0.05% over 1 month but component replacement restored values to original levels. This deterioration was not readily identified by reference to daily quality assurance results but was highlighted by observation of the 'spillover' (recording of high energy x-rays in the low energy window) and ratio of counts in air for the high and low energy x-rays.

2.4 Objective 2: Evaluation of the Lunar Expert-XL Bone Densitometer

2.4.1 Radiation Dose Assessment

An Expert-XL was installed in the author's department in 1996 primarily for research applications. As part of the commissioning and acceptance testing, a detailed dose assessment was conducted (Paper 1). Scatter doses to the operator for the various scan modes is shown in Table 2.3.

Scan Mode	Tube Current	Exposure Time	Dose rate at 1 m	Dose at 1 m	Scan Limits for 7.5 μSvh^{-1} dose rate
Whole body	1.5 mA	231.3 s	36 μSvh^{-1}	2.31 μSv/scan	26 scans/day
A.P. Spine (fast)	5 mA	16 s	120 μSvh^{-1}	0.53 μSv/scan	112 scans/day
Lat. Spine Morph.	5 mA	38 s	120 μSvh^{-1}	1.27 μSv/scan	47 scans/day
R. Femur (fast)	5 mA	14.4 s	120 μSvh^{-1}	0.48 μSv/scan	125 scans/day

Table 2.3 Scatter doses at 1 m from centre of scanning table

With an expected workload of 4 patients per hour, it was suggested that steps be taken to reduce the dose to the operator. This could include increasing the operator's distance from the scan table or installing a protective screen. The radiation dose to the patient was also found to be higher than for pencil beam DXA systems but appeared to be proportionate to the added clinical benefits of improved resolution and availability of MXA (Table 2.4).

Scan Mode	Tube Current	Scan Time	Field Width	Scan Length	Effective Dose	Effective Dose per mAs
AP spine (fast)	5 mA	16 s	17.3 cm	20 cm	59 μSv	0.74 μSv/mAs
AP right femur (fast)	5 mA	14.4 s	14.7 cm	18 cm	56 μSv* 40 μSv**	0.78 μSv/mAs* 0.56 μSv/mAs**
Lateral spine morphometry	5 mA	38 s	14.4 cm	38 cm	71 μSv	0.37 μSv/mAs
Whole body (Medium)	1.5 mA	131.3 s	4 sweeps covering the whole body		75 μSv	0.38 μSv/mAs

*assumes ovary within primary field, **assumes ovary outside primary field

Table 2.4 Effective doses to patient from standard procedures on Lunar Expert-XL

A decision was taken to install a lead glass screen to ensure scatter doses to the operator were kept as low as reasonably achievable.

This work is cited by 11 other authors in international peer-reviewed journals*. The work is also cited by the IAEA (International Atomic Energy Authority: rpop.iaea.org/RPOP/RPoP) on their website under information for Health Professionals on radiation protection of staff using DXA and by Health Canada under the section on Environmental and Workplace Health (www.hc-sc.gc.ca).

2.4.2 Image Resolution of the Expert-XL

A further study was designed and carried out to determine spatial resolution of the various scan modes using commercially available resolution test patterns (Paper 2). Spatial resolution is a measure of an imaging systems ability to distinguish between small features usually determined by how close lines can be together and still be resolved.

Fan-beam densitometry distorts and magnifies the lateral (x-axis) dimension of the image by an amount dependent on the relative positions of x-ray tube, object and detector. Conventional cone-beam radiographs distort both lateral and longitudinal dimensions. The lateral and longitudinal resolutions achieved for each scan mode under standard operating conditions are shown in table 2.5.

Scan Mode	Scan mode	Lateral Resolution Median (range) lps/mm	Longitudinal Resolution Median (range) lps/mm
AP spine	5 mA Fast	0.9 (0.7-1.0)	0.8 (<0.6-0.9)
	5 mA Turbo	0.9 (<0.6-0.9)	<0.6 (<0.6)
	2 mA Fast	0.8 (0.6-0.9)	0.8 (<0.6-0.9)
	2 mA Turbo	0.9 (<0.6-1.0)	<0.6 (<0.6)
AP Femur	5 mA Fast	0.9 (0.8-1.0)	0.9 (0.7-0.9)
	5 mA Turbo	0.9 (0.8-1.0)	<0.6 (<0.6)
	2 mA Fast	0.9 (0.8-1.0)	0.8 (0.7-0.9)
	2 mA Turbo	0.9 (0.8-1.0)	<0.6 (<0.6)
Hand	1 mA Fast	1.0 (1.0-1.2)	1.0 (1.0-1.0)
Forearm	1 mA Fast	1.0 (1.0-1.2)	1.0 (0.9-1.0)
Morphometry	5 mA Fast	1.0 (1.0-1.2)	0.7 (<0.6-0.7)

*Resolution in lps/mm = 1/resolution in mm

Table 2.5 Image resolution of the Expert-XL

* Citation searches throughout the thesis were performed using Web of Science and exclude those with which the author was involved

The test pattern used (07-541 Nuclear Associates, Carle Place, NY) contains 15 sets of lead line pairs arranged horizontally and vertically covering a range of 0.6 to 3.4 line pairs per millimetre. Resolution was found to be about 1mm, which is around half that of the older technology pencil beam DXA systems but not as good as that stated by the manufacturers. Resolution was found to be affected by thickness of attenuator and bed height but even the optimal resolution attainable (0.83mm) does not approach that of standard radiographic procedures which reach 3.5 lps/mm (0.29mm) for lateral spine imaging[20].

More research was required to inform decisions around the potential clinical use of the additional functionality of this DXA equipment. Further reports in peer-reviewed journals by 8 other authors cite the work presented above.

2.4.3 Accuracy and Precision of the Expert-XL

The evaluation work carried out on the pencil beam DPXL systems was repeated on the Expert-XL fan beam densitometer under the author's supervision. The findings demonstrated that errors due to tissue thickness could be minimised through use of appropriate scan modes but that these were not as recommended by the manufacturer at the time. The optimal scan modes were found to be the 5mA fast mode for most patients and 2mA fast for those with less than 15 cm soft tissue within the scan region (Abstract 2). These gave the most consistent results over a range of tissue thicknesses rather than the high precision turbo scan modes which were introduced by the manufacturers to improve precision (Figure 2.8).

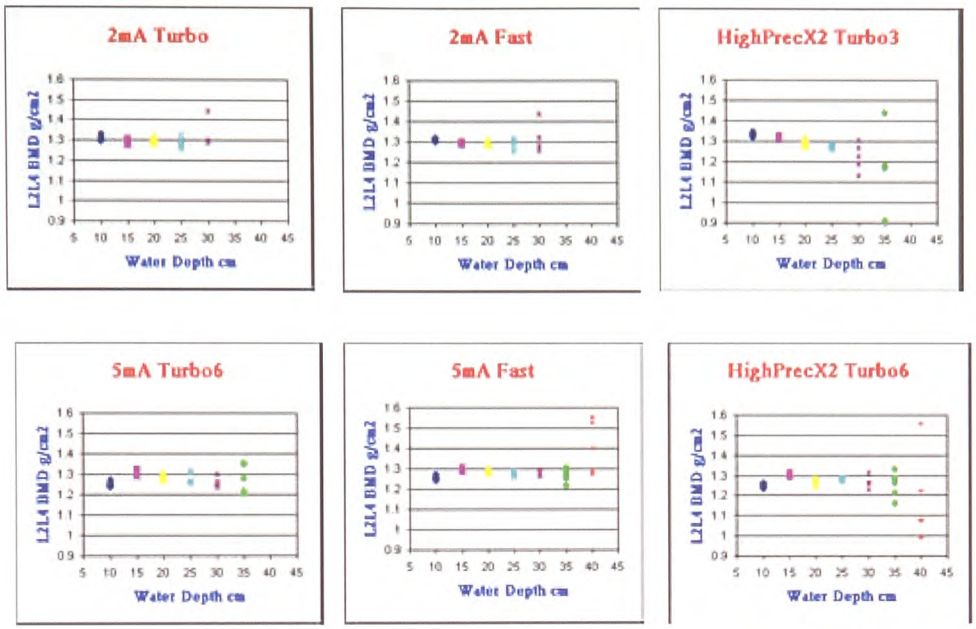


Figure 2.8 BMD (L2-L4) of Lunar Spine Phantom using varying depths of water at each scan mode.

As a consequence, the fast scan modes continued to be used for routine clinical application in the author's department.

The work above was conducted using phantoms and tissue mimicking material which may not accurately reflect precision attainable in patients. There was a need to derive in-vivo precision in-house for the population involved in order to determine whether a change in BMD during longitudinal follow-up is statistically significant and to help determine appropriate follow-up intervals.

Although bone protective treatments are proven to be effective through large, international phase III clinical trials, many clinicians still prefer to have demonstrable evidence of effectiveness on the individual. There is also a requirement to monitor some patients on drugs known to have a detrimental effect on bone. Hence, many requests are made for longitudinal measurements to monitor change in BMD.

To avoid unnecessary radiation exposure of patients attending for routine bone density assessment, the data accumulated on patients participating in clinical trials involving the Expert-XL was utilised. Two cohorts were analysed by the author, 121 post-menopausal women undergoing repeat spine BMD (with repositioning) as part of the trial and 27 post-menopausal women with repeat spine and hip data (Abstract 3).

Study group	Age	Mean spine BMD gcm^{-2}	sd	rms %CV
27 females	52.6 (45 to 60)	1.127	0.177	1.69
121 females	62 (54 to 65)	1.079	0.184	2.19

Table 2.6 In-vivo precision results for 2 study groups on the Expert-XL. Scan mode 5mA fast with repositioning between scans.

The precision as percent coefficient of variation (%CV) for spine BMD on the Expert-XL was found to be between 1.7% and 2.2% depending on the mean BMD of the study population (Table 2.6).

Precision of hip BMD for the 27 subjects, mean hip T-score of -0.6, was 0.94 at the total hip site or 1.46 for femoral neck. However, hip BMD was performed using a hip positioner (Osteodyne HPS) as required by the study protocol and therefore may not represent in-vivo precision using standard recommended procedures.

The precision of spine BMD is poorer than that of 0.7% to 1.6% reported for the pencil beam systems so the recommendation was that for routine assessment of spine BMD, the pencil beam system was preferred due to improved precision and lower radiation dose.

The work on the Expert-XL confirmed the higher spatial resolution but at a higher radiation dose and lower precision compared to the pencil beam devices. The Expert-XL was therefore utilised for research applications and vertebral morphometry (see 2.6.2) where improved spatial resolution outweighed the increased radiation burden and reduced precision.

2.5 Objective 3: Evaluation of Lunar Prodigy Bone Densitometers

A Prodigy was installed in the author's department in 2001 as a replacement for a Lunar DPXL. The Centre still housed another DPXL and the Expert-XL. The proposal was for the Prodigy to supplement the DPXL in providing the routine clinical service and that patients formerly scanned on the decommissioned DPXL would be transferred to the Prodigy.

2.5.1 Radiation Dose Assessment of the Prodigy

A radiation assessment of both patient dose and scatter dose to the operator was conducted (Abstract 4). The scatter dose to the operator was found to be 3 μSv/h which confirms that stated by the manufacturers. The radiation dose from the Prodigy was too low to utilise the anthropomorphic phantom as used for the dose assessment on the Expert-XL(see 2.4.1). Hence, skin entrance doses only were determined using an ionisation chamber under a water phantom. The dose to patients using each of the scan modes was also found to be similar to that in the proprietary literature (Table 2.7).

Scan Mode	Tube Current (mA)	Scan time (sec)	Skin entrance dose (μGy)	
			Our results	Manufacturer's literature
Ap spine: thick	3.000	55	98	83
AP spine: standard	3.000	29	43	37
AP spine: thin	0.750	29	10	9

Table 2.7 Radiation dose to patients using available scan modes on the Prodigy.

2.5.2 Precision of the Prodigy and Correlation with DPXL and Expert-XL

In-vitro and in-vivo precision of BMD using the Prodigy densitometer was determined by the author. Short-term in-vitro precision was calculated using 10 repeat scans, with repositioning, on one day of the Lunar aluminium phantom and a Hologic phantom (Abstract 4). Precision was found to be 0.3% for both phantoms. Long term precision was determined by analysis of the daily phantom scans over a period of 1 year. This was found to be 0.4% using the Lunar phantom and 0.5% using the Hologic phantom. Precision is therefore better than

that for the DPXL and Expert-XL systems.

Due to the possibility of patients being transferred from another scanner within the department following equipment failure or replacement, daily scanning of one aluminium phantom and one Hologic phantom on all systems in the department was introduced for cross-calibration purposes.

	Lunar Spine Phantom				Hologic Spine Phantom		
	n	Mean L2L4BMD gcm^{-2} (SD)	CV(%)		n	Mean L1L4BMD gcm^{-2} (SD)	CV(%)
Prodigy	226	1.257 (0.005)	0.40		135	1.170 (0.006)	0.51
DPXL	224	1.279 (0.009)	0.71		132	1.226 (0.050)	0.44
Expert-XL	226	1.281 (0.010)	0.78		135	1.154 (0.007)	0.60

Table 2.8 In-vitro Inter-Machine Comparison

Using the aluminium phantom, BMD was found to be 1.7% below that determined for the same phantom measured on the DPXL and 1.9% below that on the Expert-XL (Table 2.8).

The phantom BMD results above only provide a guide to the machine differences and may not be applicable in patients[21]. The author therefore carried out in-vivo studies to determine precision and inter-machine variability between the Prodigy and DPXL (Abstract 5).

Site	Mean BMD (gcm^{-2})	Mean Difference (gcm^{-2})	Precision (CV%)
Spine L2-L4	1.016	-0.004	0.9
Femoral Neck	0.841	0.001	1.4
Total Hip	0.872	0.004	1.0

Table 2.9 In-vivo precision of the Prodigy from duplicate scans of 36 women

Precision was determined using repeat spine and hip BMD of 36 post-menopausal women recruited for a randomised clinical trial. The women were aged 46 to 67 years and all were osteopenic (T score -1 to -2.5). In-vivo

precision was found to be 0.9% at spine, 1.4% at femoral neck and 1.0% at Total Hip (Table 2.9) which is comparable to that reported for the pencil beam DXA systems and better than that of the Expert-XL fan beam densitometer as presented previously (section 2.4.3 and Table 2.6).

The findings above led to the Prodigy being chosen as the densitometer of choice for replacement of the remaining DXA scanners as the time arose.

The in-vivo difference between the scanners was calculated using a group of 31 postmenopausal women attending as part of a nine year longitudinal study of peri- and post-menopausal changes in BMD (Abstract 5). The women underwent BMD of spine and hip on both the Prodigy and DPXL. The inter-machine variability was found to be not so large at the spine (0.6% below) than for the in-vitro study. However, femoral neck BMD was 2% higher on the Prodigy than on the DPXL (Table 2.10).

SITE	**DPXL MEAN (SD) BMD gcm^{-2}**	**PRODIGY MEAN (SD) BMD gcm^{-2}**	**MEAN DIFFERENCE (95%C.I.)**
Spine L2-L4	1.101 (0.166)	1.095 (0.175)	-0.007 (-0.073 to 0.059)
Femoral Neck	0.850 (0.120)	0.868 (0.124)	0.018 (-0.089 to 0.125)

Table 2.10 BMD of 31 women scanned on both the DPXL and Prodigy on the same day.

These results demonstrate that cross calibration based on phantom studies is inappropriate. However, because of the wide variation in in-vivo BMD between the scanners, cross calibration may only be of use in large population studies and not for correction of individual results.

Others have since reported slightly better in-vivo agreement between a DXPL and Prodigy[22] with a mean difference at spine of 0.001 gcm^{-2} and at femoral

neck of -0.003 gcm^{-2}. Cross calibration results are therefore not transferrable to other scanners even where the same types of scanner are being compared.

The work outlined in this section demonstrates the improved precision and lower radiation dose of the Prodigy systems compared to the Expert-XL. Consequently, the Prodigy systems were chosen as the devices to be used for routine assessment of spine and hip BMD in the author's department.

2.6 Development of DXA Quality Assurance Devices

2.6.1 Objective 4: Development of a Phantom for Hand BMD Quality Assurance

The aim was to develop a phantom to assess precision and linearity of the DPX and DPXL densitometers at the low BMD values (0.3 to 0.9 gcm^{-2}) found in the hand (Paper 3). The phantom should also be robust enough for use in monitoring long-term precision. Through pilot work carrid out by the author using various thicknesses of aluminium and Perspex representing bone mineral and lean soft tissue respectively, appropriate dimensions of the simulated phalanges were determined. These were embedded in a Perspex block drilled precisely to fit. A phantom suitable for use with the original pencil beam DXA devices was designed by the author and constructed in-house (Figure 2.9).

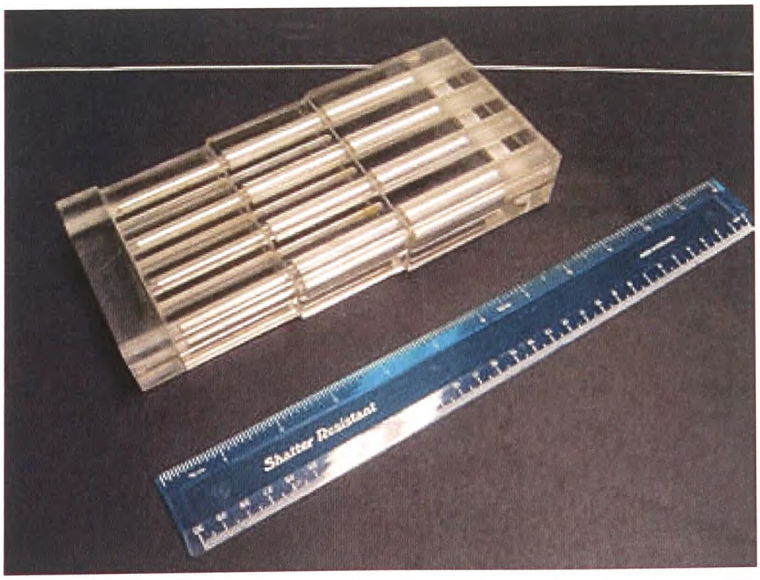


Figure 2.9 Hand Phantom for DXA

scan mode		metacarpals		proximal phalanges		distal phalanges	
	n	BMD gcm^{-2} mean (s.d.)	%CV	BMD gcm^{-2} mean (s.d.)	%CV	BMD gcm^{-2} mean (s.d.)	%CV
det.med	10	0.947(0.021)	2.21	0.564(0.019)	3.34	0.310(0.008)	2.62
det.slow	10	0.949(0.017)	1.88	0.575(0.023)	4.07	0.306(0.006)	1.83
hires.med	5	0.984(0.002)	0.17	0.606(0.002)	0.39	0.279(0.002)	0.74
hires.slow	5	0.990(0.003)	0.33	0.609(0.004)	0.71	0.266(0.003)	1.04

Table 2.11 Mean BMD and precision for the 3 regions of interest using each of the 4 scan modes of Lunar small animal software

As can be seen from Table 2.11, the trend of increasing BMD with increasing resolution for the higher BMD regions is reversed in the low BMD 'distal phalanges' region of the phantom. This was found to be due to failure of the software to identify all of the bone equivalent area as bone.

scan mode		metacarpals		proximal phalanges		distal phalanges	
	n	AREA cm^2 mean (s.d.)	%CV	AREA cm^2 mean (s.d.)	%CV	AREA cm^2 mean (s.d.)	%CV
det.med	10	60.81(0.85)	1.39	22.57(0.37)	1.62	6.48(1.15)	17.82
det.slow	10	61.21(0.78)	1.28	22.45(0.39)	1.75	6.47(1.49)	23.01
hires.med	5	61.81(0.06)	0.10	22.74(0.01)	0.03	12.85(0.11)	0.88
hires.slow	5	61.84(0.06)	0.10	22.70(0.03)	0.14	13.64(0.42)	3.10
actual projected area		62.40 cm^2		22.76 cm^2		17.29 cm^2	

Table 2.12 Mean area and precision for the 3 regions of interest using each of the 4 scan modes of Lunar small animal software. Actual projected areas containing 'bone' within each region are indicated.

The areas determined by the software to contain bone or bone equivalent material within the distal phalanges region of the phantom were underestimated by 21% to 62% depending on scan mode (Table 2.12).

This work demonstrated that the DPX systems were incapable of detecting BMD below a threshold of around $0.3gcm^{-2}$, a value which is not unusual in-vivo in the hand. Improved recognition of low bone density values was achieved with the higher resolution fan beam Lunar Expert-XL (section 2.4) introduced in the mid

1990s and the hand phantom was redesigned for use with this system. As a consequence, the Expert-XL was chosen as the system to be used for measurement and monitoring of BMD of the hand. This work has been cited by 3 other authors.

2.6.2 Objective 5: Development of a Phantom for Quality Assurance of MXA

The Expert-XL DXA systems are mounted on a C-arm that can be rotated to enable lateral imaging of the spine with the patient in the supine position (Figure 2.10).

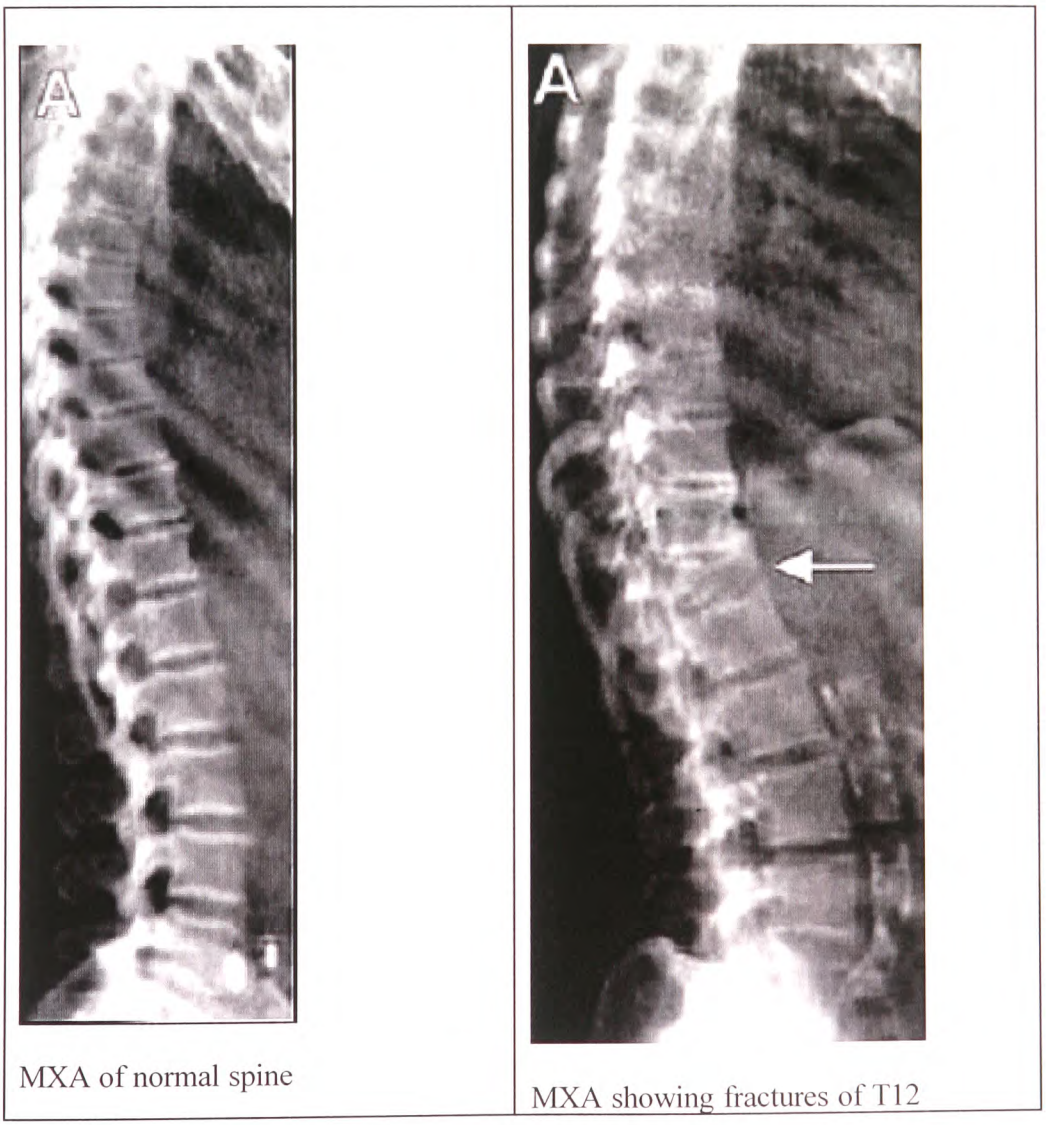


Figure 2.10 Lateral spine images produced using an Expert-XL scanner

A morphometry phantom suitable for MXA was designed by the author and constructed in-house (Figure 2.11). The phantom consists of 3 components; a Perspex torso-mimicking block with a drilled core and two aluminium and Perspex inserts (Paper 4). The inserts are constructed of 12 cylinders of aluminium with phosphor-bronze endplates, one column being of regular shaped cylinders designed to check alignment, positioning and mechanical movements and one of irregular cylinders representing vertebral deformities.

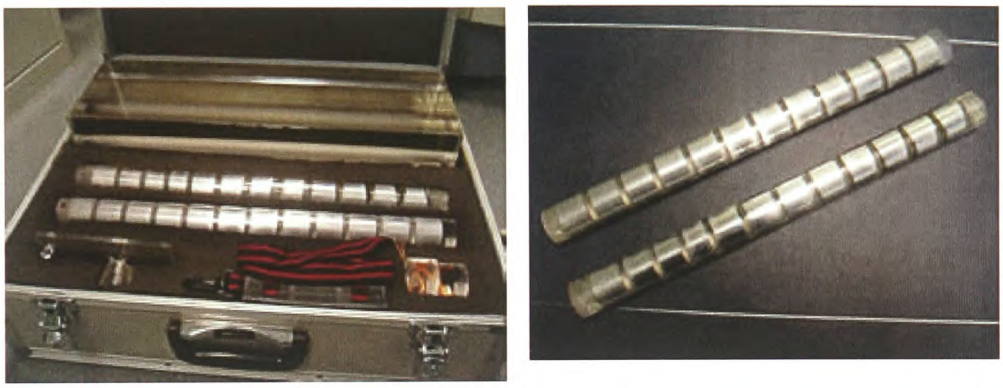


Figure 2.11 MXA Phantom

Use of this phantom on the Expert-XL fan beam densitometer demonstrated a precision of 0.6% to 1.1% in measurement of vertebral height depending on the complexity of the shape. There was also found to be a consistent underestimate of vertebral height by 5% but this may not be clinically significant as the degree of vertebral deformity is generally determined relative to the heights of the 2nd to 4th lumbar vertebrae (L2-L4).

The Hull MXA phantom was the first of its kind and proved to be invaluable for assessing the accuracy of MXA, inter- and intra-operator variability and to monitor long-term precision. The phantom continues to be used weekly on all DXA scanners in the Centre. The work is cited by 4 later reports evaluating precision and application of the VFA technique.

A further study was designed and carried out under the author's supervision using the morphometry phantom to examine the effect of patient positioning, scoliosis and kyphosis on the MXA technique using the Expert-XL. This work demonstrated that kyphosis of up to 6% had a minimal effect on MXA but scoliosis of greater than 4.6% significantly affects the measurement (Paper 5).

The work earned the young investigator award from the National Osteoporosis Society in 1998 for the research assistant Jonathan Thorpe and is cited by Rea *et al.* in their report on development of a similar phantom in 2001[23].

Results of the work above helped inform the decision to introduce MXA into routine clinical practice in Hull, initially on selected patients with strong indication for vertebral fracture but later as a screening tool in all those over 65 years attending for DXA. These two strategies were later compared and the findings presented in the Clinical Application chapter of this thesis (section 3.6: Paper 14). The work was also cited by the International Society for Clinical Densitometry in the development of their position statements on the use of VFA[24].

2.7 Peripheral Densitometry

2.7.1 Objective 6: Evaluation of the PIXI heel DXA device

A peripheral DXA device, the PIXI, was purchased for the Centre in 1999 by the local charity OSPREY. A proposal was made to the local Osteoporosis Strategy Group that the device could be utilised for community based BMD in females aged 70 to 75 years who may benefit most from the convenience and reduced travel. Prior to this, an assessment of in-vivo precision of the device was required which was determined using duplicate measurements on 105 women aged 70 to 76 years. This was found to be 1.9% compared to 1.6% for spine BMD in the same population (Abstract 6).

As the WHO definition of osteoporosis is not applicable to the heel, a working threshold was also derived by the author which best predicted BMD status at spine and hip. The 105 subjects also underwent spine and hip BMD (Lunar Prodigy). The correlation between heel and spine or hip BMD was found to be 0.54 and 0.53 respectively compared to 0.64 for spine versus hip BMD. The agreement between the techniques was examined using Bland-Altman plots to compare T-scores (Figures 2.12 and 2.13). These display scatter plots of the differences in the T-scores between the two techniques against the mean of the two measurements. Horizontal lines are drawn at the mean difference, and at the limits of agreement (mean difference +/- 1.96 times the standard deviation of

the differences). The results indicate a significant difference between the two measurements (mean diff. spine-heel -0.25; p=0.05 and mean diff. hip-heel -0.32; p<0.01). The mean difference is also correlated with BMD both for spine-heel (r=0.337; p<0.01) and hip-heel (r=0.282; p<0.01).

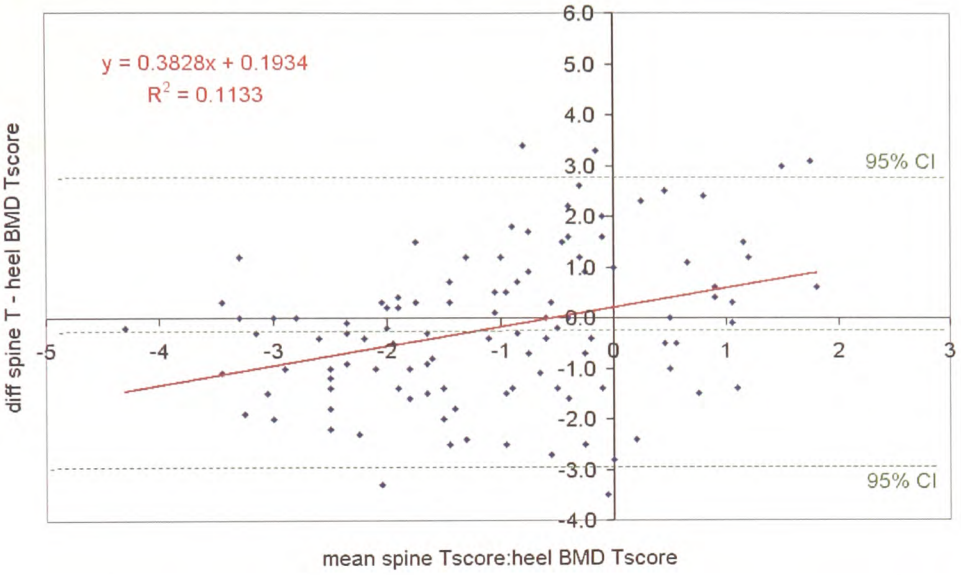


Figure 2.12 Bland-Altman plot of difference against mean of spine and heel BMD

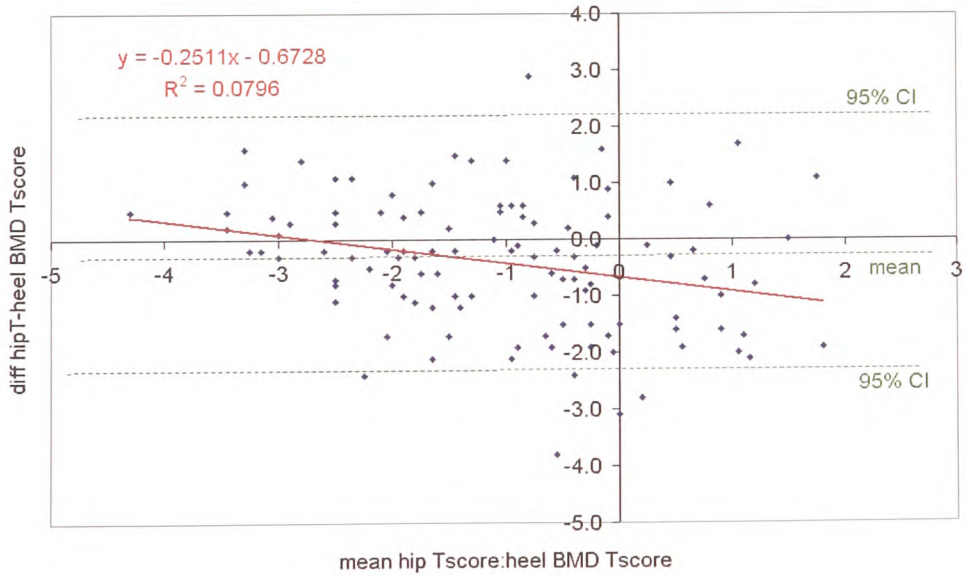


Figure 2.13 Bland-Altman plot of difference against mean of hip and heel BMD

Using ROC analysis a T-score threshold of around -1.7 for heel BMD by PIXI was found to minimise the proportion of patients who would be over- or under-referred if the technique was used as a pre-screen for DXA spine and hip. Sensitivity and specificity for osteoporosis at spine or hip using a threshold of -1.7 is 72% and 74% respectively. This also identified the same proportion of the population as being at risk as by using a T-score of -2.5 for spine and hip BMD. These findings are in concordance with later published work[25]. The T-score threshold of -1.7 was utilised for the community-based pilot project of screening elderly women in the Hull area. The results of the work were awarded with **Best Poster** at an international conference in Rio de Janeiro in 2000.

2.7.2 Objective 7: Evaluation of the DXL Calscan

A study was carried out by the author to determine the in-vitro and in-vivo operating conditions of the DXL Calscan and to consider its clinical role, through comparisons with both axial BMD and with peripheral BMD using the PIXI (Paper 6).

The effectiveness, application and stability of the Calscan were examined through a series of *in-vivo* and *in-vitro* tests. The device proved to be easy to use, stable when used within recommended environmental conditions and involved a very low radiation dose of less than 0.1μSv. In-vivo precision at 1.2% was slightly better than that for the PIXI (1.9%). Triage thresholds were also determined to categorise patients for *'reassurance'*, *'referral'* for spine and hip DXA or *'treatment'* in accordance with the recently published National Osteoporosis Society guidelines on peripheral DXA[26] (Figure 2.14)

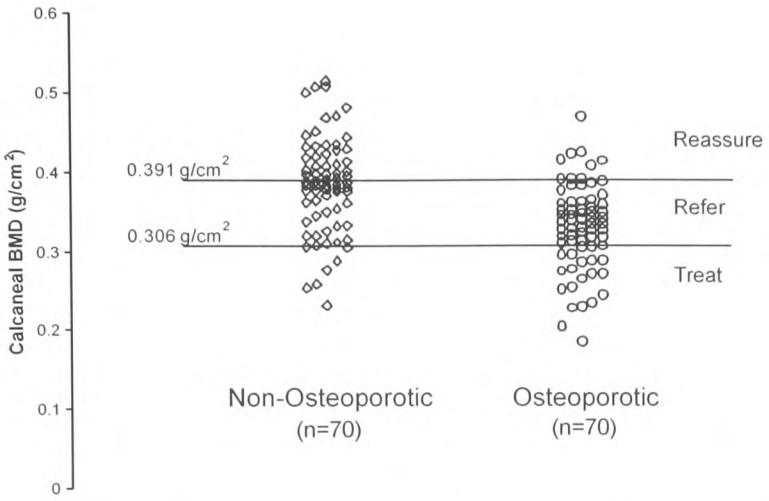


Figure 2.14 DXL Calscan upper and lower triage thresholds for the non-dominant heel.

From the subjects in the study, 53% were found to have a heel BMD within the 'refer' category. However, this sample does not represent the ratio of osteoporotic to non-osteoporotic as seen in routine clinical referrals. Correction for this indicates around 40% of patients would require referral for confirmation of bone status by spine and hip DXA requiring therefore heel DXA cost per case to be less than 60% of a spine and hip measurement to result in a net saving.

The findings of this study are incorporated in the list of device specific thresholds collated by the National Osteoporosis Society[27]. The work has also been cited by 2 other authors conducting further evaluation of the device and is cited in the position statement on pDXA by the International Society of Clinical Densitometry[28].

2.7.3 Objective 8: Evaluation of the Alara Metriscan

An evaluation of the Alara Metriscan hand densitometer was also carried out to determine the in-vitro and in-vivo operating conditions and to determine triage thresholds as for the Calscan (Paper 7). One hundred and seventy women attending for routine spine and hip DXA also underwent measurement of the hand using the Metriscan. The device was simple to operate and radiation dose to the patient and scatter dose to staff was very low. In-vivo precision at 1.42% was similar to that found for heel BMD.

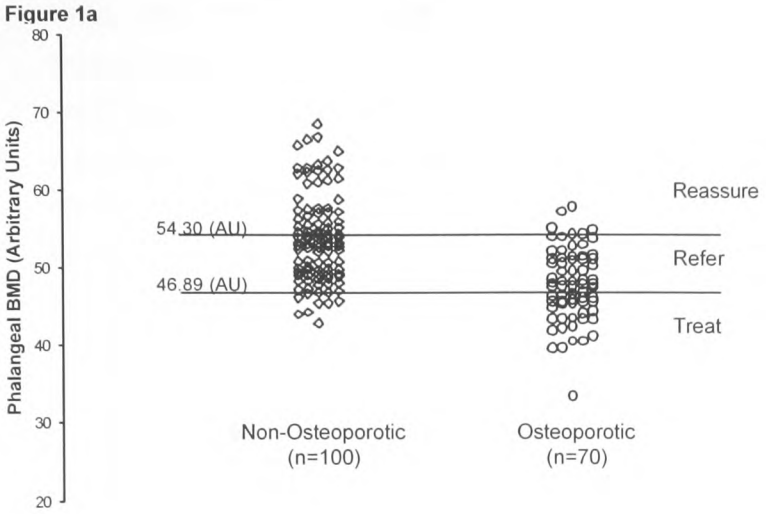


Figure 2.15 Alara Metriscan upper and lower triage thresholds for non-dominant hand

The triage thresholds, determined in accordance with the NOS guidelines[26], identified around 44% of patients requiring referral for confirmation of bone status by spine and hip DXA (Figure 2.15). This is a larger proportion than that when heel BMD is used as a triage tool.

The findings of this study are incorporated in the list of device specific thresholds collated by the National Osteoporosis Society[27].

2.8 Summary

The work presented above addressed the objectives set out in section 2.2.

Objective 1 – Evaluation of the DXPL densitometers was carried out and the following results presented:

a) Accuracy – phantom BMD was within +/- 2% of manufacturer's value which confirms acceptable level of accuracy of BMD measurement.
b) Long term precision was found to be 0.8% which demonstrates good reproducibility and stability of the equipment over time.
c) Effect of tissue depth and composition – Although errors in BMD could be introduced with increasing or decreasing tissue depth,

representing over-/underweight patients, these were minimised by using the appropriate scan modes available. The automated selection of scan mode by the software based on patient weight and height was observed in practice to be unreliable hence a procedure was introduced for measurement of tissue depth within the scan region and manual selection of appropriate scan mode.

Measurement of BMD is not significantly affected by variations in fat to lean composition of soft tissues that are encountered in clinical practice. However, discrepancy in soft tissue composition within the projected bone region as opposed to that either side can significantly affect BMD. Further work is needed to determine the clinical significance of this especially in view of the increasing proportion of yellow (fatty) marrow with age. In 2009, Blake *et al.* demonstrated that a change in vertebral marrow fat content from 0 to 100% led to a difference in BMD equivalent to approximately 1.3 T-score units[29]. However, this did not significantly affect the ability of spine BMD to predict fracture risk.

d) Inter-machine variability - There was found to be a significant variation between the machines which reinforced the recommendation that follow-up scans where needed should be performed as far as possible on the same scanner.

This work provided a benchmark for comparison and established the techniques for evaluation of later densitometry equipment. The experience gained in identifying the factors that influence accuracy and precision led the author to establish rigorous quality assurance procedures locally and ensure operators were well trained and following standard operating procedures. This approach was later incorporated into a national training scheme as described in section 4.3.

Objective 2 – evaluation of the Expert-XL:

a) Radiation Dose – effective dose to the patient was found to be between 40 and 75 μSv depending upon scan site and scan mode used. These are higher than that for the pencil beam DPXL systems.

Scatter dose to the operator was found to be around 0.5 μSv for

spine and hip BMD but higher for lateral or whole body scanning. Depending on patient throughput, scan mix, and room size, a lead glass screen may be required to ensure operator dose remains below recommended limits.

b) Precision – In-vivo precision of the spine was found to be 1.7 to 2.2% which is poorer than for the DPXL (0.7 to 1.6%).

c) Resolution – Using a test pattern, resolution was about 1mm which is much better than that of pencil beam systems.

These findings supported the continued use of the DPXL machines for routine BMD to keep doses as low as reasonably practicable. The Expert-XL was reserved for research and applications where the improved resolution and additional functionality such as lateral vertebral assessment outweighed the additional radiation burden.

Objective 3 – evaluation of the Prodigy Densitometers:

a) Precision – in-vitro precision using the Lunar spine phantom was 0.4% and the Hologic phantom 0.5%. In-vivo precision based on a group of osteopenic women was 0.9% at spine, 1.9% at femoral neck and 1.0% at the total hip site. This is similar to that of the pencil beam DPXL systems and better than the wide angle fan beam Expert-XL.

b) Radiation dose - scatter dose to the operator was found to be 3 μSv/h. The skin entrance dose to the patient for a standard spine scan was 43 μGy which is similar to that stated by the manufacturers (37 μGy). This equates to an effective dose of approximately 6 μSv.

c) Comparison with DPXL – using a cohort of 31 postmenopausal women scanned on both Prodigy and DPXL on the same day, spine BMD on the Prodigy was found to be on average only 0.6% below that using the DPXL but hip BMD was 2% higher.

The findings supported the continued use of the Prodigy in routine clinical practice.

Objective 4 – development of a hand phantom:

a) Construction - A phantom for use in quality assurance of hand BMD by DXA was designed initially for use on the DPXL.

b) Use on the DPXL – use of the phantom on the DPXL demonstrated that they are incapable of detecting BMD below a threshold of around 0.3 gcm^{-2}, a value which is not unusual in-vivo in the hand.

c) Redesign for Expert-XL - The phantom was later redesigned to suit the Expert-XL which had improved recognition of low bone density values. As a consequence, the Expert-XL was chosen as the system to be used for measurement and monitoring of BMD of the hand.

Objective 5 –evaluation of MXA technique:

a) Phantom development – A phantom was designed and constructed for evaluation and use in quality assurance of MXA. Using this phantom on the Expert-XL demonstrated a precision of 0.6% to 1.1% in measurement of vertebral height depending on the complexity of the shape. There was also found to be an underestimate of vertebral height by 5% which may not affect diagnostic value as the degree of vertebral deformity is generally determined relative to the heights of the 2nd to 4th lumbar vertebrae.

b) Patient positioning effects – results using the phantom also demonstrated that kyphosis of up to 6% had a minimal effect on MXA but scoliosis of greater than 4.6% significantly affects the measurement.

Results of the work helped inform the decision to introduce MXA into routine clinical practice. The exclusion criteria in the standard operating procedure for MXA include patients with severe kyphosis or scoliosis. The work also paved the way for further research presented in the next chapter on the appropriate targeting of the technique (section 3.6).

Objective 6 – evaluation of the PIXI peripheral DXA system:

a) In-vivo precision - Using duplicate measurements on 105 women aged 70 to 76 years, mean heel T-score -1.0 (-1.2 at spine) precision was found to be 1.9%.

b) Relationship with axial BMD – The same subjects underwent spine and hip BMD on the Lunar Prodigy. The correlation between heel and spine or hip BMD was found to be 0.54 and 0.53 respectively compared to 0.64 for spine versus hip BMD.

c) Threshold for clinical use - A T-score threshold of -1.7 was found to optimise use of the PIXI in a pre-screen role.

The findings confirmed that the device was suitable for use as an adjunct to an axial DXA service and enabled a community-based pilot project of screening elderly women in the Hull area to proceed.

Objective 7 – evaluation of the DXL Calscan heel densitometer:

a) Accuracy and Precision – Phantom BMD did not differ from the manufacturer's reference value. Short term precision was found to be 0.8% and long-term derived from daily phantom scanning over a 6 month period was 0.7%.

b) Radiation dose – dose to the patient was found to be very low at less than 0.1μSv and scatter dose to the operator well below annual dose limits.

c) In-vivo precision – using duplicate measurement on 140 subjects with a mean heel T-score of -2 (-2 at spine), precision was 1.2% which is slightly better than that for the Lunar PIXI (1.9%) especially considering the lower bone density of the Calscan subjects.

d) Triage thresholds – thresholds were determined to categorise patients for *'reassurance'* (above T-score of -1.4), *'referral* for spine and hip DXA (T-score between -1.4 and -2.7) or *'treatment'* (below -2.7).

The findings of this study helped development of operating protocols and provided guidance for users on patient management based on the BMD result. The triage thresholds are incorporated in the list of device specific thresholds collated by the National Osteoporosis Society[27].

Objective 8 – evaluation of the Metriscan hand densitometer.

a) Radiation dose – dose to the patient was found to be very low at less than 0.1μSv and scatter dose to the operator well below annual dose limits.
b) In-Vitro Precision – short term precision was 0.2% and long-term derived from daily phantom scanning over a 6 month period was 0.3%
c) In-Vivo Precision - using duplicate measurements on 170 subjects, mean T-score -1 (-2.0 at spine) precision was found to be 1.4%.
d) Triage thresholds - thresholds were determined to categorise patients for *'reassurance'* (above T-score of -0.5), *'referral'* for spine and hip DXA (T-score between -0.5 and -2) or *'treatment'* (below -2).

Again, this work helped with consideration of appropriate placement of this technology in the clinical arena and provided patient management guidance based on the result. As for the DXL Calscan, the derived triage thresholds for the Metriscan are incorporated in the NOS device specific thresholds.

In summary, this chapter demonstrates the authors contribution to knowledge of factors associated with the measurement of BMD by axial DXA using pencil, fan-beam and semi-fan-beam technology and by peripheral DXA and the potential of additional functionality of spine morphometry.

CHAPTER 3

CLINICAL APPLICATION OF DXA

3.1 State of Knowledge at the Time

3.1.1 Identification of High Risk Groups

At the time DXA was introduced, there was debate over the appropriate target population for this diagnostic test. The natural history of osteoporosis, having a long lead time, presents an opportunity to detect using DXA those at risk prior to the first fracture and offering preventative treatment. As low bone mass is symptomless, this primary prevention approach would entail population screening. However, a report commissioned by the Department of Health concluded that on the basis of evidence at the time, population screening of postmenopausal women was not justified[30]. They cited lack of scientific trials on screening to prevent fractures, lack of evidence of Hormone Replacement Therapy effectiveness in fracture prevention, poor compliance with treatment and concerns over the precision and predictive accuracy of BMD by DXA. Studies had demonstrated that reduction in BMD was associated with an increase in fracture risk[31 32 33] although an overlap in BMD between hip fracture patients and age matched controls was reported[34]. Population screening is thought to be unjustified in view of the reduced sensitivity and specificity for predicting fragility fracture, associated radiation burden and cost.

Guidance was needed on appropriate use of this new technique within a clinical setting.

3.1.2 Factors associated with low Bone Mass

There was a growing body of knowledge on factors associated with attainment of peak bone mass and bone loss. Peak bone mass was reported as being determined by genetic potential modified by hormonal status, exercise and nutrition. Studies of twins demonstrated that genetic factors were more important in youth but were later superseded by environmental factors[35]. Athletes who became amenorrhoeic were found to have lower BMD[36] although the mode of action of sex hormones on the skeleton was unknown. Association between bone mass and physical activity was reported[37, 38] and studies

identified the role of calcium in skeletal health[39] [40]. There was general consensus that age and oestrogen deficiency were strongly associated with bone loss[41] whilst low calcium intake[42] and reduced physical activity[43] were thought to be contributory factors.

More research was required into factors which may be associated with low bone mass and hence increased fracture risk.

3.1.3 Hormone Replacement Therapy

Oestrogen is known to play a role in bone turnover[44] with loss of oestrogen leading to an imbalance of bone formation and resorption with a consequent loss of bone mass[45]. At the time of introduction of DXA, Hormone Replacement Therapy (HRT) was the treatment of choice for prevention of post menopausal bone loss to the extent that universal treatment of low bone mass with HRT had been advocated[46]. HRT reduces bone loss[47] and confers other benefits in terms of relieving menopausal symptoms. However, reports in 2002-03 from the Women's Health Initiative (WHI) study demonstrated increased incidence of breast cancer, cardiovascular disease and stroke in women taking HRT[48]. The increased risks were small amounting to an additional number of cases per 10,000 of 8, 7 and 8 respectively. The media focussed on these negative findings at the expense of the positive confirmation that HRT reduces the risk of hip fracture[49]. However, poor adherence to treatment has been reported but these studies were generally in a small sample over short periods of time[50].

Evidence at the time suggested that HRT needed to be taken for at least 5 years to confer lasting benefits on bone[47] [49]. However, due to the reported adverse effects, shorter courses of HRT for the control of menopausal symptoms were favoured. The effect of such intervention on bone in the medium term was unknown.

More information was required on compliance to HRT and effectiveness of short courses in preventing bone loss.

3.1.4 Utility of MXA

Vertebral fractures were reported as being the most common osteoporotic fractures[8] with prevalence rising to 25% in women over 50 years[9] although many of these fractures go undetected. These fractures are associated with a significant increase in risk of future vertebral and other fractures[10 51 52]. Lack of knowledge of vertebral fracture status can thus lead to a substantial underestimate of fracture risk. The addition of baseline spine x-ray information substantially improves the ability of risk factor models to predict an incident fracture[53] but spine x-rays are not a practical method of screening for fracture.

As reported in 2.6.2 above, technological and software developments enable modern DXA scanners to be used for vertebral fracture assessment although there were no recommendations as to when this additional diagnostic procedure should be used.

3.2 Outline of the motivation and significance of the work undertaken

The motivation for the work presented in Appendix IV was to contribute to the debate over the appropriate use of DXA and MXA and add to the understanding of factors thought to be associated with bone loss and fracture risk. The findings helped with the development of local guidelines for referral and management of osteoporosis and contributed to the growing body of knowledge though publication and presentations. The areas to be investigated reflected the requirements of the clinical service and interests of the investigator.

The following objectives were set to help address the gaps in knowledge detailed above in this chapter.

3.2.1 Objective 1 was to investigate the feasibility of population screening by DXA in a peri-menopausal population. This included examining the technical capabilities of the equipment, establishing action thresholds, assessing the support of healthcare professional in Primary Care and willingness of women to participate and comply with the treatment regime.
This objective is addressed in Section 3.3.

3.2.1 Objective 2 was to examine factors that may be associated with attainment of peak bone mass or bone loss. The study on effect of Coeliac disease on BMD was of interest due to the finding of a high proportion of previously undiagnosed Coeliac disease in those found to have low BMD as part of the logistical feasibility study.
This objective is addressed in Section 3.4.

3.2.2 Objective 3 was to explore factors associated with adherence to HRT and the effect of short courses of treatment on BMD.
This objective is addressed in Section 3.5.

3.2.3 Objective 4 was to use the vast database and experience accumulated on use of MXA to help determine appropriate and effective use of the technique.
This objective is addressed in Section 3.6.

3.3 Objective 1: Feasibility of population screening by DXA

A logistical and technical feasibility study was undertaken by the author which involved screening by DXA of 6282 peri-menopausal women (Paper 8). As a consequence of the equipment evaluation reported previously (section 2.3) a rigorous quality assurance programme, procedures and protocols were introduced to optimise accuracy of the results. The feasibility study which lasted 3 years demonstrated that the pencil beam DXA systems were reliable, precise and capable of examining up to 12 patients a day with a down time for maintenance or malfunction of only about 2 days per year. Age matched reference ranges were established by the author and a threshold derived for recommendation of HRT for bone protection. Screening was acceptable to the GPs (61 of 62 participated) and the patients (83% attendance). However, 2 year compliance with bone protective treatment (HRT) was only 48% primarily due to a return to cyclic bleeding or a fear of breast cancer.

The author played a key role in eliciting the support and participation of the general practitioners in the screening programme. This collaboration evolved into the formation in 1993 of the Osteoporosis Strategy Group of which the author was a founder member and latterly vice-chair. Using the findings of the study agreed indications for bone densitometry were established and local

guidelines developed[54] supported by the local health purchasing authority. The criteria for referral are broadly in line with those later introduced by the National Osteoporosis Society[55] and the Royal College of Physicians[56]. However, the appropriate use and interpretation of DXA remains an area for debate[57 58].

3.4 Objective 2: Effect of Coeliac Disease on BMD

Coeliac disease is a malabsorption syndrome which may affect the absorption of calcium from the diet. Previous studies identified biochemical and skeletal disturbances thought to be due primarily to impaired absorption of Vitamin D leading to malabsorption of calcium and other smaller studies had suggested a link between coeliac disease and BMD.

A study of 81 women with coeliac disease was carried out by the author (Paper 9). All underwent BMD of spine and hip by DXA and each was carefully matched to a control subject from an age-matched population if post-menopausal or from a young adult group if pre-menopausal. This process was performed to exclude confounding factors. The study confirmed that coeliac disease has an adverse effect on BMD even after adjusting for height, weight, menopausal status and menopausal age. Interestingly, in the pre-menopausal group this manifested itself only in hip BMD which could be due to the increased proportion of cortical bone at this site. The exact mechanisms were not fully understood and although more is now known about the disease process and its effect on bone, there remain unanswered questions[59]. However, a review in 2008 of published work involving a total of 20,995 coeliac patients, confirmed a significant association between bone fractures and coeliac disease[60].

There were few non-adherers to a gluten free diet so it was not possible to assess the influence of diet on BMD. This required a larger prospective study. Later studies demonstrated a beneficial effect on bone in children with coeliac disease adhering to a gluten free diet[61].

The results of the author's study led to the recommendation that DXA at spine and hip be performed at the time of diagnosis of coeliac disease to act as a baseline. This was added to the local referral criteria for DXA. The work is cited by a guideline development group[62] and by 41 other authors.

3.5 Objective 3: Investigation of the Influence of HRT

3.5.1 Factors affecting compliance

Diagnosis of low bone mass in peri-menopausal women is fruitless if there is resistance to the treatment offered to prevent further bone loss. HRT was the treatment of choice at the time but some reported low adherence rates in women found to have low bone mass. Paper 10 describes results from a 5 year follow-up conducted by the author of 1,462 women with low BMD diagnosed during the screening programme described in 3.3 above. As part of the study, data were recorded on a computerised database of BMD, patient demographic and physical details and medical and social factors thought to influence BMD. Software and hardware changes during the study required corrections to be made to the follow-up data to allow for effect on BMD. Adherence to HRT at 5 years was found to be 61% with the largest discontinuation rate being during the first 2 years. This was one of the highest reported adherence rates in a clinical setting which may be attributable to knowledge of fracture risk and regular follow-up. The findings may not be representative of the larger population as 36% of the study group were lost to follow-up. However, others have since confirmed that close follow-up improves compliance[63].

3.5.2 Effect on BMD

Following the adverse findings of the WHI study in 2002, HRT was no longer recommended for prevention of postmenopausal bone loss. It is still licensed for the relief of menopausal symptoms although these courses of treatment tend to be shorter than the 5 years recommended for bone protection. Paper 11 describes a study of effectiveness of short-term HRT in 587 women followed up at 2, 5 and 9 years after screening as part of the feasibility study discussed in 3.4 above. Results suggest that the protective benefits conferred on bone by a short course of HRT (2 to 4 years) remain for up to 5 years after the treatment is withdrawn. Women taking a short course of HRT after the menopause on average had no significant loss in BMD over 9 years.

3.6 Objective 4: Utility of MXA

As a consequence of the previous validation work on MXA reported above (2.6.2), the technique was introduced in the author's centre with the approval of the local Osteoporosis Strategy Group. Initially, only those presenting for spine and hip DXA with reason to suspect a fracture were considered but from 2005 all women over 65 years attending for DXA underwent a vertebral fracture assessment (VFA) if physically able to do so. Using data collected on the initial 'targeted' group (6,388 women) and the later 'routine' group (2,176 women), the author compared the two screening strategies (Paper 12). This was the largest study reported on routine use of VFA. It was found that routine screening detected vertebral fractures in 20% of the women over 65 years attending for DXA and that 77% of these were previously undiagnosed. Targeted screening minimised resource implications as only 5% of those attending for DXA underwent VFA but this strategy identified less than 10% of those with a vertebral fracture.

Although the paper was published less than 1 year ago, the work has already been cited once by El Maghraoui *et al.* studying the prevalence and risk factors of vertebral fractures using VFA in asymptomatic Moroccan women[64]. The findings also led to further work to try and refine the selection of women for VFA to maximise detection of fractures whilst minimising resource implications[65].

3.7 Summary

The work on clinical application of DXA presented in Appendix IV addressed the objectives set out in section 3.3.

Objective 1 - The feasibility of population screening by DXA was undertaken with the following outcomes:

a) The pencil beam DXA systems were reliable, precise and capable of supporting population screening.
b) Age matched reference ranges were established and a threshold derived for recommendation of HRT for bone protection.

c) Screening was acceptable to the GPs (61 of 62 participated) and the patients (83% attendance).
d) 2 year compliance with bone protective treatment (HRT) was 48%.

The study led to the establishment of local agreed indications for bone densitometry.

Objective 2 - The Effect of Coeliac Disease on BMD was investigated. A study of 81 women with coeliac disease demonstrated an adverse effect on BMD even after matching for height, weight, menopausal status and menopausal age.

Objective 3 – HRT compliance and effect on BMD was explored:

a) 5 years adherence to HRT in 1,462 with low BMD was 61% with the largest discontinuation rate being during the first 2 years.
b) Short courses of HRT can have long-term benefits on bone.

Objective 4 - The data accumulated on over 8,000 women undergoing vertebral fracture assessment was examined. This demonstrated vertebral fracture prevalence of 20% in women over 65 years, 77% of which were previously undiagnosed which would have led to a substantial underestimate of their future fracture risk. Attempts to target VFA at only those with indications of a possible vertebral fracture proved to be ineffective.

This work confirmed that the strategy to consider VFA in all women over 65 years presenting for DXA was more effective than targeted screening and secured the resources required to continue this approach.

In summary, this chapter demonstrates the author's contribution to knowledge of the appropriate role of DXA and VFA in a routine clinical environment.

CHAPTER 4

STANDARDS IN DIAGNOSIS OF OSTEOPOROSIS

4.1 BACKGROUND

Some sites in the UK were fortunate to acquire DXA systems in the late 80's and early 90's, often through charitable donations or from pharmaceutical companies who had a vested interest in encouraging diagnosis and hence increased prescribing of bone protective treatments. Being x-ray based, these systems were usually located within radiography or nuclear medicine departments where staff had the knowledge and expertise of x-ray production and detection and radiation safety. The earlier systems were mostly operated by radiographers or medical physics technicians who merely required device specific instruction. Since osteoporosis is a multi-causal and therefore multidisciplinary disease, there remains a range of professions and disciplines involved in diagnosis and management with no legislation on minimum training requirements and, until recently, no guidance on use of the diagnostic equipment. Peripheral bone densitometers in particular are marketed as being simple to use, the implication being that specialist technical or scientific knowledge is not required. As a relatively new diagnostic technique, measurement of bone mineral density is not included in the syllabus of existing medical technology courses. There is no legislation restricting use of such devices except where ionising radiation is involved[66 67] which can be fairly readily satisfied but difficult to enforce. Clinicians in both primary and secondary care faced with an unmet need for diagnosis with limited resources are turning to available staff and low cost equipment. With little guidance to the contrary, commissioners and administrators support these developments. The consequences are that highly specialised equipment used to aid the clinician in making treatment decisions sometimes lies in inexperienced hands. Without appropriate guidelines and training, there is a potential for misuse and misdiagnosis.

As minor changes in BMD are known to reflect major changes in fracture risk, attention to standards in use of DXA is critical to ensure optimal precision, minimum follow-up interval and to maximise the possibility of detecting the true treatment effect.

4.2 Outline of the motivation and significance of the work undertaken

The motivation for the work presented in Appendix V was to contribute to improving the standards of clinical DXA services in the UK.

Objective 1 – Raise the background knowledge and technique of DXA operators.
This objective is addressed in Section 4.3.

Objective 2 – Provide guidance on use of DXA in the clinical environment.
This objective is addressed in Section 4.4.

4.3 National Osteoporosis Society Training Scheme (NOS)

The need for improving standards of bone densitometry was raised at meetings of the Bone Densitometry Forum of the NOS. Consequently, a sub-group was formed to consider the feasibility of introducing a national training scheme that could be accessible to all healthcare professionals involved in operating DXA equipment. The result was the NOS National Training Scheme for bone densitometry delivered and examined by the NOS Bone Densitometry Certification Panel (BDCP). The author is a founder member, contributor to the contents of the rules and regulations and syllabus (Appendix V: Scheme Literature) and is a lecturer of the course. The scheme is now endorsed by the major professional bodies concerned, the College of Radiographers and the Institute of Physics in Engineering and Medicine and recognised by the Royal College of Physicians.

4.3.1 Course Outline

The aim is to improve standards for bone densitometry measurements through an accredited scheme that is recognised by the appropriate professional colleges and institutions. The course is open to operators who have undergone initial on-site training and have at least 6 months experience of using the diagnostic equipment in a clinical setting. The scheme consists of a 2 day lecture course which must be attended, including an IRMER module to meet the requirements of the Ionising Radiation in Medical Exposure Regulations. Those wanting to continue to certification must pass an examination followed by submission of a portfolio of work in bone densitometry.

4.3.2 Lecture Programme

Training is provided in the theory and application of bone densitometry measurement techniques through a two day taught course which includes scientific, technical and clinical lectures and panel discussions (Appendix V: Lecture Programme). The author delivers two of the lectures, participates in the panel discussions and assists with on-site arrangements.

Feedback is sought from the students at the end of each lecture course. This has been positive and constructive in helping the BDCP to develop and adapt the course to changing needs.

4.3.3 Supporting Material

A Fundamentals Booklet is provided which includes sections on 'The Bone Densitometry Service' and 'Data Management and Report Generation' written by the author (Appendix V). The former chapter aims to provide the student with a summary of the fundamentals of a good service from receipt of request to patient handling and quality assurance through to final reporting. The chapter is well referenced and indicates relevant legislation that must be adhered to. The second chapter provides advice on data management and security and the production of a meaningful report to the referrer. This booklet is now provided in CD format. Printed copies of all slides used in the lectures are collated in a course manual which is provided to all candidates.

Candidates are also encouraged to undertake recommended reading before sitting an examination. The author contributed to the development and regular review of a reading list.

4.3.4 On-line Examination

As candidates attend the course from all over the UK, the exam is carried out on-line at several sites simultaneously across the country. The NOS commissioned the University of Glamorgan to construct the online National Bone Densitometry Online Testing System (NBDOTS) during 2002. The examination is a Web-based application that uses the Internet and Web browsers to deliver the tests anywhere in the world. It is based on the online software 'Perception' (QuestionMark http://www.questionmark.com). The BDCP produce 3 sets of objective testing questions which reflect the modules of the

lecture course: Core Clinical, Core Technical and DXA. The author has contributed questions to the Core Technical and DXA sections and evaluated and selected those on the Core Clinical section. Both multiple choice and multiple response formats are used, with all correct responses required in the latter for a full mark for the question. Following the candidate's submission of their completed answers, results are automatically marked against pre-defined correct solutions.

NBDOTS produces an analysis of the performance of each examination and its questions. The range of difficulty is determined by the proportion of candidates answering correctly. The ability of each question to discriminates between a high scoring group (the top 27% by assessment score) and a low scoring group (the bottom 27% by assessment score) is also determined. These factors enable review of the questions by the BDCP in order to consider exclusion of misleading or confusing questions when reviewing results. Correlation of a question score to overall examination score is also derived which, if very low, may indicate the question should be excluded.

Being computerised enables results and detailed analysis of results to be available to the examiners almost instantaneously. This successful exam format has been developed in conjunction and with the continued support of the Faculty of Advanced Technology, Department of Computing and Mathematical Science of the University of Glamorgan. The author contributed to the format and content of the on-line examination and acts as invigilator at one of the examination sites.

4.3.4 Portfolio Submission

Candidates passing the exam are able to submit a portfolio of practical work for assessment by the examination panel. The author contributed to decisions regarding the content of the portfolio which is designed to test the candidates understanding of equipment quality assurance and the results printout, their scan and analysis technique and the role of DXA in patient management. Due to the popularity of the scheme with around 100 registrants per course, a number of portfolio markers are required. In order to minimise variability, the author developed a marking scheme and associated instruction for markers. Also, all portfolios failing to meet the required pass marks are subject to a second, independent review.

To date 589 have attended the lecture course with 264 successfully completing the scheme and achieving certification. Employers are now including successful completion of the scheme as a requirement for new employees in bone densitometry and the qualification is also proving useful within the new knowledge and skills framework of professional development.

4.4 Guidelines

Writing groups of the Bone Densitometry Forum currently chaired by the author were nominated to develop guidelines and position statements associated with DXA. These documents are subject to regular review to reflect emerging evidence and changing clinical guidelines.

4.4.1 Guidelines for the Provision of a Clinical Bone Densitometry Service

This document included in Appendix V is designed by the author to provide a benchmark for practitioners, commissioners and service providers when developing or comparing DXA services. The numbered list with key recommendations summarised at the beginning delivers the minimum requirements for a clinical DXA service in a succinct, easy to read format. A service conforming to these standards would meet current guidance on the appropriate use of DXA and legislation governing ionising radiation and data protection. Compliance with Clinical Governance and Health and Safety issues would also be addressed. The reader is directed to sources of supporting information about each of these topics.

4.4.2 Position statement on the reporting of dual energy x-ray absorptiometry (DXA) bone mineral density scans

This document with contributions from the author provides the first national guidance on interpretation and reporting of spine and hip DXA scans. The aim is to reduce the confusion and variability of interpretation of the results. There is an emphasis on checking the image for artefacts or positioning errors that may affect the result. Advice is given on the role of T- and Z-scores in diagnosis, interpretation and patient management. The document also includes guidance on appropriate follow-up intervals and provides a proposed structure for reporting of DXA scans. This document was published in 2004 and is currently

undergoing revision to incorporate new developments particularly around the proposal to incorporate other risk factors in producing a fracture risk score for the individual and how to use this in therapeutic decision making.

4.5 Summary

The initiatives presented are aimed at improving standards in the diagnosis and monitoring of the osteoporotic patient and meet the objectives set out in section 4.2.

Objective 1 – The NOS National Training Scheme for bone densitometry has helped raise the background knowledge and understanding of the diagnosis and treatment of osteoporosis amongst operators, clinicians and managers. Examination of portfolios of practical work has assured operator technique meets appropriate standards or has been improved through detailed feedback and resubmission.

Objective 2 – The guidance documents provide concise, evidence based recommendations for users, providers and commissioners of DXA services. Both documents are scheduled for revision within 2009/10.

CHAPTER 5

CONCLUSION

5.1 Meeting the Aim

The original aim of the author was to help integrate DXA within the clinical environment in a safe, effective and efficient manner. The results of the work presented in this thesis achieve this aim from three aspects summarised below.

5.1.1 Independent Equipment Evaluation

Dual Energy X-ray Absorptiometry (DXA) was introduced in the late 1980s followed in by the introduction introduced in the early 1990's of new therapeutic agents for bone protection. With the adoption of BMD by DXA in1994 to provide a definition of osteoporosis[75], there was a rapid deployment of DXA equipment. This was a new fast developing quantitative digital imaging technique in medicine which had been the subject of little independent evaluation and validation.

The work presented in this thesis provides an independent evaluation of the technical capabilities and limitations of the technology. The findings were applied locally when designing appropriate accommodation with consideration being given to environmental conditions to ensure equipment stability and room layout to meet Ionising Radiation regulations. The work also provided a benchmark of equipment precision and factors that may affect accuracy.

The phantoms developed for hand and vertebral morphometry were the first available for quality assurance of these techniques and provide a means of evaluating the accuracy, precision and long-term stability. This helped the author's centre become be an early implementer of VFA which enabled further research on the clinical use. Evaluation of the peripheral DXA techniques contributed to advice on their appropriate role and to the proposed triage thresholds.

Accuracy of DXA equipment is initially assured through calibration in the factory against known bone standards. The phantom supplied with the equipment acts

as a secondary standard to check the accuracy of the scanner calibration throughout its operational life. Repeated phantom scans on the same day will also provide a measure of precision and regular scans of the phantom, preferably every working day, will provide an indication of any drift of the results over time. As part of the commissioning and acceptance testing of new equipment, in-house precision should be determined both *in-vitro* and if possible *in-vivo* using the now recommended method of root mean square standard deviation as percent coefficient of variation (rms CV%)[68]. From this can be calculated the least significant change which must be exceeded in serial measurement to be reasonably confident of a true change. This will help determine the minimum follow up interval.

The manufacturer supplied phantoms do not reflect all factors encountered *in-vivo* that may affect accuracy and precision. Findings of the work presented in this thesis demonstrate the influence of tissue thickness and non-uniformity of lean and fat tissue composition across the region of interest. Excessive or reduced tissue thickness may lead to an over- or under-estimate of BMD respectively, although the errors may be minimised through use of appropriate scan modes. The age-related increase in the proportion of fat in bone marrow may lead to an underestimate of BMD and there is currently no mechanism for correcting this error. Although much of the work was conducted on older technology, these characteristics are a feature of x-ray attenuation at the energies used and therefore largely applicable to all DXA devices. The phantom used for routine quality assurance does not capture these potential sources of error. More thorough evaluation of new generation DXA devices is recommended using a range of phantoms reflecting the variability of BMD and soft tissues encountered *in-vivo*. This should preferably be an independent evaluation for each new model released and should include determination of the effects of tissue depth and variation of soft tissue composition across the region of interest at a range of BMDs encountered in clinical practice. A knowledge of the anticipated errors in accuracy and precision for each scenario will help when interpreting the DXA results and considering patient management.

5.1.2 Informing Clinical Application

The identification of a new, preventable or treatable disease had educational, logistical and financial consequences for the National Health Service in the UK.

It was unclear in the early days whether the technique would be acceptable, which patient groups should be offered a DXA scan, whether it could be utilised to monitor BMD changes and whether this would influence medical management. There was also little data on what factors were associated with attainment of bone mass or bone loss.

The work on equipment evaluation provided the baseline characteristics of accuracy, precision and potential sources of error of the technique. This helped in establishing a rigorous quality assurance procedure and developing standard operating procedures for patient preparation and scan technique to optimise results. Consequently, the population screening feasibility study proved successful the findings of which were essential in establishing the local service in 1992. Local guidelines were developed based around referral criteria derived from this study and DXA interpretation was initially based on the local population reference derived. With the later addition of manufacturers' reference data and the introduction of the T-score concept, the WHO definition was adopted although other risk factors for fracture were taken into consideration when recommending treatment.

The investigation on the effect of coeliac disease contributes to the growing body of knowledge of factors thought to be associated with low bone mass. The studies of HRT demonstrate good adherence to treatment and a sustained beneficial effect on bone of short courses, a timely report in view of concerns over long-term use of HRT. More recent safety data on HRT have become available, including re-analyses of results from the Women's Health Initiative trial which suggest the increased risks of breast cancer, stroke and cardiovascular disease reported previously are associated with increasing age when commencing HRT and duration of treatment[69]. Also, the risks are significantly reduced following cessation of treatment[70]. The current recommendations from the Royal College of Obstetricians and Gynaecologists (www.rcog.org.uk) support the use of HRT in the immediate post-menopause for as short a time as needed for control of menopausal symptoms. The Medicines and Healthcare Products Regulatory Agency (www.mhra.gov.uk) support its use for prevention of osteoporosis only in women who are unable to use alternative bone protective therapies. The findings reported in this thesis, indicate that a short course of HRT in the immediate post menopause, such as used for control of symptoms, can have long term benefits for bone health.

Following the technical evaluation of VFA, research was conducted on the clinical role of the technique which provides advice to others based on the largest cohort of patients at the time. The findings indicate that the best strategy is to consider VFA in all women over 65 years where possible.

5.1.3 Improving Standards

Due to the multi-causal and hence multidisciplinary nature of osteoporosis, operators, users and clinicians are from a range of professions and disciplines. As a relatively new diagnostic technique, measurement of bone mineral density was not included in the syllabus of existing medical technology courses. Also, inclusion of osteoporosis diagnosis and management in the training programmes of relevant professional bodies may be configured to meet specific professional requirements and not address all aspect or reach all disciplines. Without appropriate guidelines and training, there is a potential for misuse and misdiagnosis.

The NOS Training Scheme has improved standards nationally as evidenced by the quality of submitted portfolios of work from DXA operators and inclusion of evidence of successful completion of the scheme within the person specification for advertised posts. The National Guidelines and Position Statements set a benchmark against which existing services can be measured and direction for those developing new services. Adherence to this guidance will ensure compliance with relevant National policies and legislation.

In summary, reliability of the equipment is assured through appropriate environmental conditions, regular maintenance and a rigorous quality assurance procedure. Together with high quality training and adherence to written procedures and protocols, this ensures reliability of clinical results. Safe use of the technology is addressed through the high standards of equipment and operating protocols and knowledge of the radiation burden to patients and staff to ensure adherence to Ionising Radiation Regulations. Targeting of appropriate populations for investigation through use of the referral criteria derived ensures efficient use of the technique.

5.2 Future Work

In the absence of a reasonably priced prophylactic therapy with no unwanted side effects, better targeting of bone protective treatments to prevent a significant proportion of fragility fractures in the most cost-effective way remains the goal. Although a measure of BMD by DXA is considered the best predictor of fragility fracture, the technique is still imperfect with a degree of overlap of those defined 'at risk' or 'not at risk' and the incidence of fracture. BMD is a quantitative measure that has been shown to be related to bone strength. However, other structural and qualitative aspects also play a role. Some work has already been done on measurement of hip structural parameters from a DXA image but more research is needed to determine whether this combined with BMD is a better predictor of hip fracture (Figure 5.1).

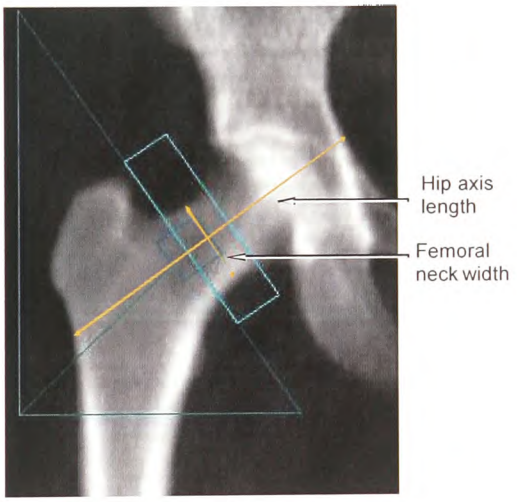
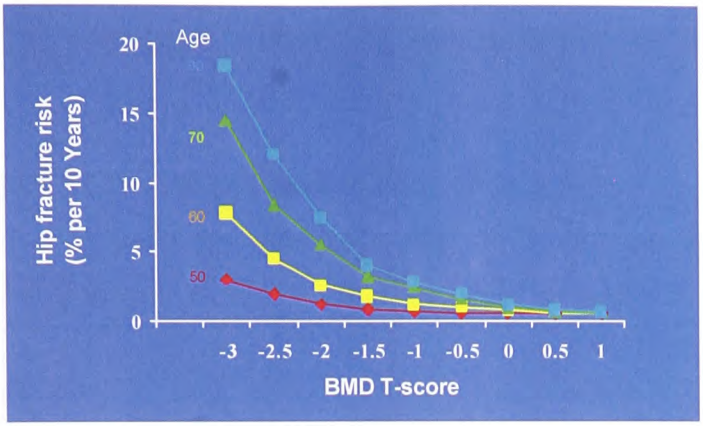


Figure 5.1 DXA image showing Hip Axis Length (HAL)

Other work is needed to refine the non-invasive in-vivo determination of bone strength.



Kanis et al, Osteopor Int 2001

Figure 5.2 Risk of hip fracture increases with decreasing BMD and increasing age

Other patient-related factors are also known to play a role independent of BMD, such as age (Figure 5.2) and prior fragility fracture, particularly vertebral fracture with 19.2% risk of further fracture within 1 year[71]. The World Health Organisation developed a computer based algorithm for calculating fracture risk which combines BMD, if available, with known risk factors for fracture (FRAX 2008: www.shef.ac.uk/FRAX). The impact of this on clinical services and patient management remains to be assessed.

Interventional techniques are available to stabilise and reduce the pain of vertebral fractures. Vertebroplasty involves injecting a material into the fractured vertebra and has been shown to reduce pain in both in the short[72 73] and long term[74]. However, a recent report in 2009 [75] suggests no benefit of the technique and others report it may lead to increased incidence of fracture particularly of adjacent vertebrae[76]. More research is needed to determine the appropriate role of vertebroplasty in clinical practice.

With advancement in technology and emergence of new evidence in the prevention, diagnosis and treatment of osteoporosis, educational needs will change. This will require regular review of the guidelines and content of courses and the mechanism of delivery. Engagement of the professional colleges and other educational providers needs to be explored and encouraged.

APPENDIX I

X-RAYS AND DUAL ENERGY X-RAY ABSORPTIOMETRY

1. PRODUCTION AND ATTENUATION OF X-RAYS

This section is included for information only as it sets the scene for the development of DXA.

1.1. Introduction

The discovery of x-rays is attributed to Wilhelm Roentgen, Professor of Physics in Würzburg, Bavaria. In 1895 he was experimenting with a cathode ray tube covered in black paper when he discovered previously unknown electromagnetic rays which were capable of passing through the paper and causing a nearby screen to fluoresce. He found the rays were able to penetrate other objects including the human body, leaving the bones and any metal visible.

1.2. X-ray Production

Modern day x-ray tubes are based on the same principle as the one used by Roentgen. A negatively charged filament is heated emitting electrons which are accelerated through an evacuated tube under the influence of a high voltage to collide with a positively charged anode (figure A1.1).

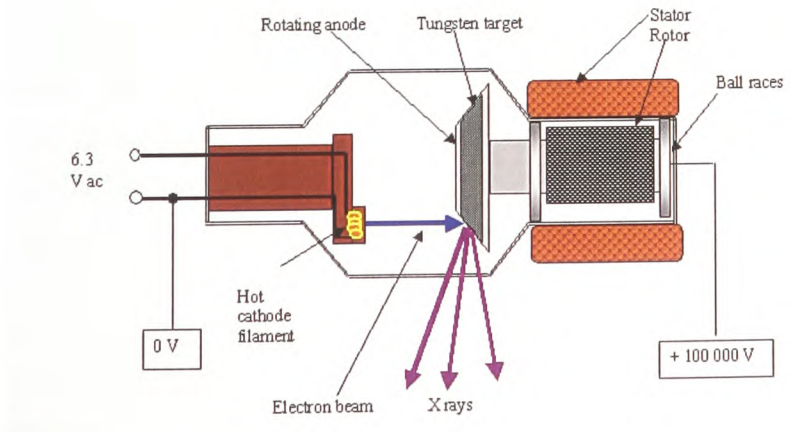


Figure A1.1 Diagram of an x-ray tube

The electrons are decelerated by the high atomic number target material, usually tungsten or molybdenum, resulting in 'Bremsstrahlung' (braking radiation) of a continuous spectrum of x-ray energies ranging from zero to the maximum voltage applied across the x-ray tube (Figure A1.2). Many of the lower energy x-ray photons do not escape due to absorption within the target material itself or within the x-ray tube. If the electrons have sufficient energy, they can knock an electron out of an inner shell resulting in the emission of characteristic x-ray photons with precise energies determined by the electron energy levels.

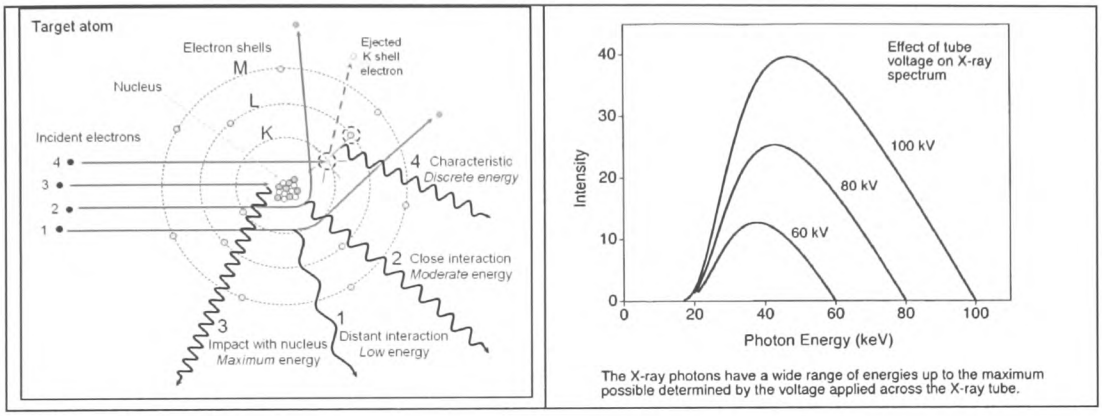


Figure A1.2 Diagrammatic representation of interactions in x-ray tube target (left) and x-ray continuous spectrum (right).

1.3 X-ray Attenuation

As the x-rays pass though the body, they are absorbed or scattered to varying degrees dependent upon the energy of the incident x-rays and properties of the material they are passing through. The primary interaction for diagnostic x-rays is the photoelectric effect which is highly dependent upon the atomic number of the material. High atomic number material will absorb more x-rays. The different absorption characteristics of tissues in the human body allows them to be distinguished from one another, providing the contrast needed for routine clinical radiography (Fig A1.3 left). The linear attenuation coefficient, which describes the proportion of x-rays absorbed per unit thickness of material, provides a measure of x-ray attenuation. Often, the mass attenuation coefficient, the attenuation per unit volume of absorbing material, is used as this is independent of material density.

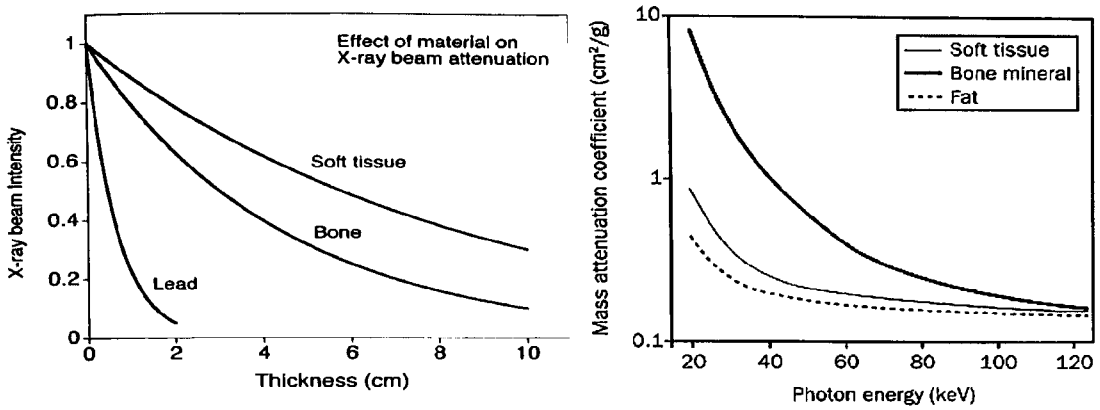


Figure A1.3 Transmission of X-rays through different materials (left) and mass attenuation coefficients of materials in the body (right)

The intensity of the transmitted x-ray beam is given by the equation:

$$I = I_0 e^{-\mu x} \qquad \textbf{Equation A1.1}$$

Where I_o is the intensity of incident x-rays, I the intensity of the transmitted x-rays and μ is the linear attenuation coefficient which is the fractional change in intensity of the incident beam per unit thickness of the attenuating material. The linear attenuation coefficient is specific for a given material of thickness x at a given x-ray photon energy. The mass attenuation coefficient μ_m is related to the linear attenuation coefficient by the density of the material:

$$\mu_m = \mu/? \qquad \textbf{Equation A1.2}$$

Equation A1.1 then becomes:

$$I = I_0 e^{-\mu ? x} \qquad \textbf{Equation A1.3}$$

The variation of the mass attenuation coefficient for bone and soft tissue differs markedly with x-ray photon energy such that the ratio is greatest at the lower energies (Figure 1.3 right). Capitalising on this, a new quantitative digital x-ray technique, Dual Energy X-ray Absorptiometry (DXA), was introduced in 1987 to determine, *in-vivo*, the density of bone, an important determinant of fracture risk. Note also from figure 1.3 that there is a slight difference in the attenuation of lean and fat tissue.

2 DUAL ENERGY X-RAY ABSORPTIOMETRY

This section provides a description of the technology studied in this thesis

2.1 Introduction

DXA was designed to provide a ***quantitative*** assessment of bone mineral, a measure of bone strength and propensity to fracture. This is unlike diagnostic radiographic equipment which is designed to optimise image resolution in order to ***qualitatively*** assess structures within the body.

2.2 Dual x-ray production

DXA is based on the assumption that there are only two materials in the body, bone and soft tissue. The differential attenuation of the two x-ray energies effectively provides two simultaneous equations (2.5: Equations A1.4 and A1.5) which can be solved to quantify the attenuation due to bone and that due to soft tissue. The x-ray energies are chosen to optimise the differential attenuation between bone and soft tissue whilst minimising the radiation dose to the patient.

Production of two energy x-rays may be achieved by rapidly switching the voltage supply to the x-ray tube between two different voltages (Figure A1.4). This technique produces two continuous spectra of x-ray energies with two different peaks around 50keV and 85keV and was adopted by one of the major manufacturers of DXA equipment (Hologic, Bedford, Massachusetts, USA). An x-ray detector records the signal for each part of the cycle. An alternative method is to use a rare earth filter (usually Cerium or Samarium) to selectively absorb x-rays of a particular energy through interactions with the electron in the inner, k-shell of the atom (k-edge filtration). The continuous x-ray spectrum is split into high and low energy parts with maximum intensities of around 40 and 70 keV. This method is used by the other major manufacturer (GE-Lunar, Madison, Wisc.).

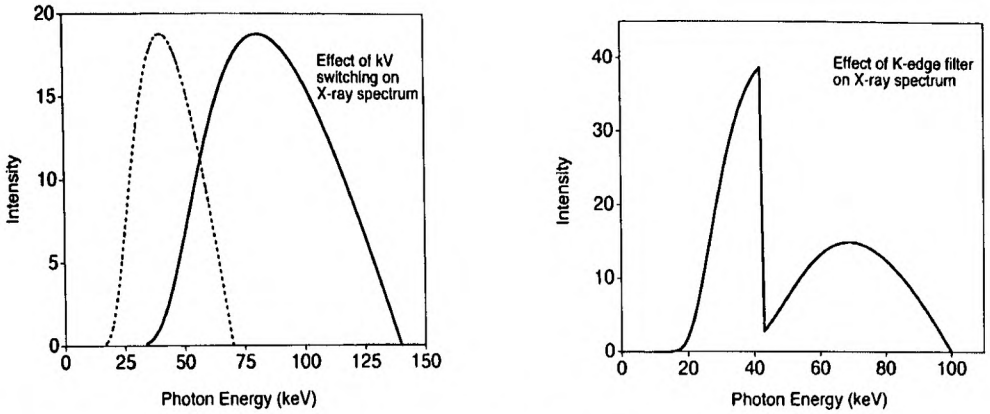


Figure A1.4 Dual energy x-rays produced by continuous switching of tube voltage between high and low values (left) or by use of a metal filter to selectively attenuate X-rays of a specific energy so splitting the continuous X-ray spectrum.

2.3 DXA Beam Shapes

The x-ray beam passes through a collimator which shapes the beam as required. Standard radiographic systems use cone beam geometry which leads to magnification and distortion towards the edges of the field of view. The original DXA systems incorporated a pin-hole collimator to produce a pencil beam of x-rays but newer systems are based on a fan beam. The Lunar Expert-XL utilises a wide angle fan beam across the width of the patient, a higher output of x-rays and an array of solid state detectors. This provides faster, higher resolution images than the pencil beam systems. The later Prodigy systems use a narrow fan beam cranio-caudally (Figure A1.5) and again solid state detectors.

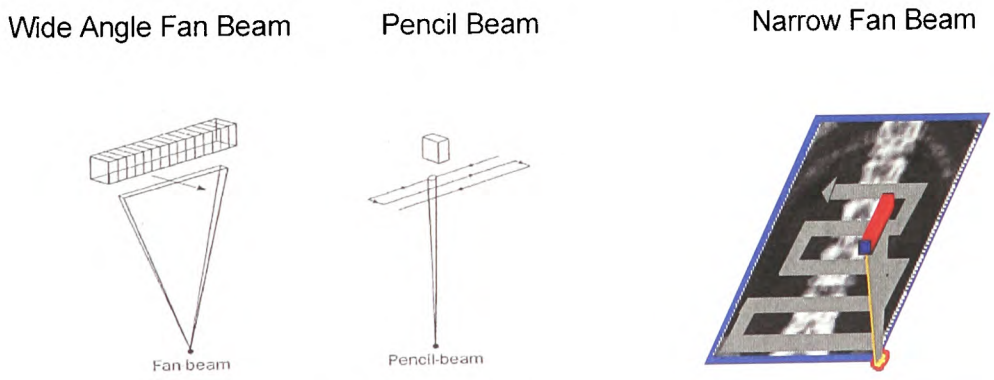


Figure A1.5 DXA beam geometry

2.4 DXA Detectors

The emitted x-rays are stopped and measured by means of an x-ray detector which for pencil beam systems is in the form of a scintillation detector (Figure A1.6). This consists of a crystal (generally NaI activated by a small amount of thallium) which converts ionising radiation into a light photon. The light photon strikes the photosensitive surface which ejects low energy electrons. These are collected and amplified through the photomultiplier tube. The size of the pulse which emerges is proportional to the energy of the x-ray photon which was absorbed in the crystal. It is therefore possible to distinguish between photons of different energy, as is required for the rare-earth filtered x-rays, using a pulse height analyzer.

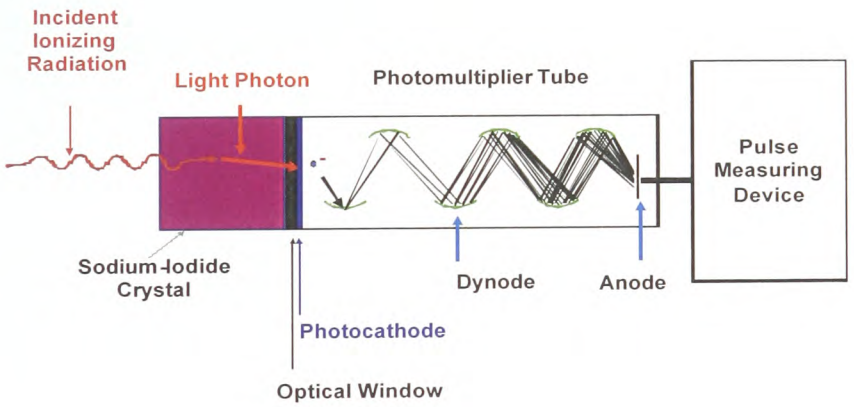


Figure A1.6 Diagram of a scintillation detector

The signals are digitally processed and assigned to a high- or low-energy x-ray window. In the rapidly-switched voltage systems, the current produced by the detector is collected during each part of the cycle. This integrated current is proportional to the intensity of the incident x-rays.

Newer, fan beam systems use an array of solid state detectors where a semi-conductor material, such as ZincCadmiumTelluride (ZnCdTe), replaces the scintillator. The x-rays are absorbed producing electron-hole pairs in the semi-conducting material. The negative and positive charge carriers move, in opposite directions, under the influence of the applied electric field to be

collected and counted electronically. The electrical pulse is proportional to the energy of the incident x-ray. These devices are more efficient and improve image resolution.

The x-ray tube and detector are mounted onto a gantry such that the two may be moved in unison by a controlled drive mechanism (Figures A1.7,A1.8).

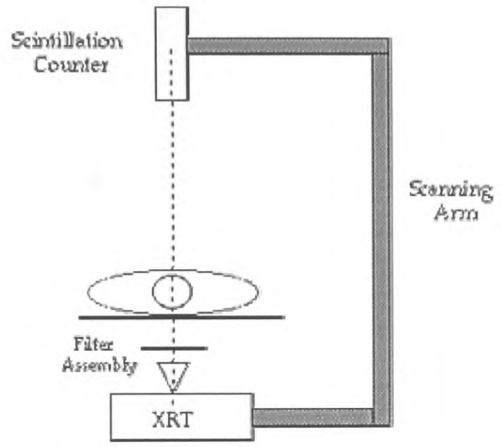


Figure A1.7 Diagram of x-ray tube and detector assembly

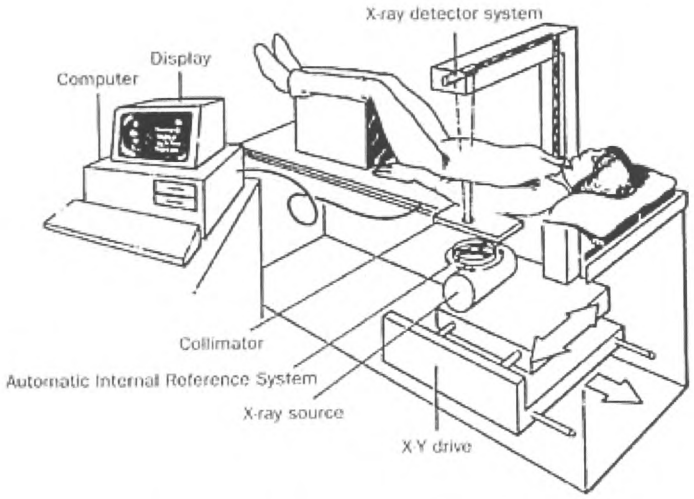


Figure A1.8 Diagram of typical DXA pencil beam system (Hologic, Bedford, Massachusetts)

2.5 Software Algorithm

Transmission profiles are effectively produced for each 'line' of the scan for the two photon energies (Figure A1.9). On passing through the human body, the low energy x-rays are attenuated more than the high energy, but especially so by bone. The high energy profile is multiplied by a factor (k) which equates the soft

tissue attenuation to that of the low energy-x-ray. This factor is derived from the ratio of attenuation coefficients of high and low energy x-rays within the soft tissue area. Subtraction of this corrected profile from the low energy profile leaves a profile of attenuation due only to bone.

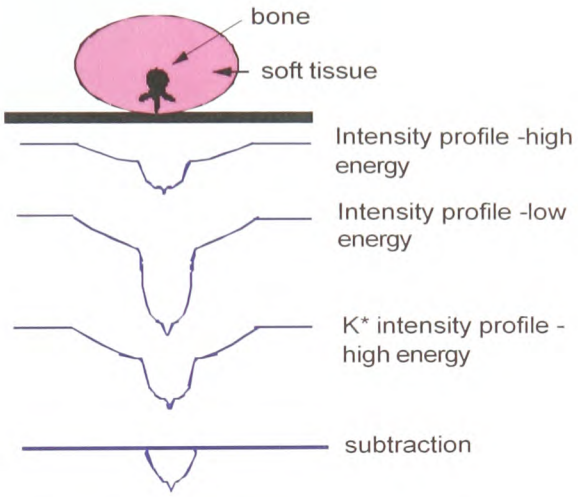


Figure A1.9 Diagram of DXA transmission profiles for high and low energy x-rays

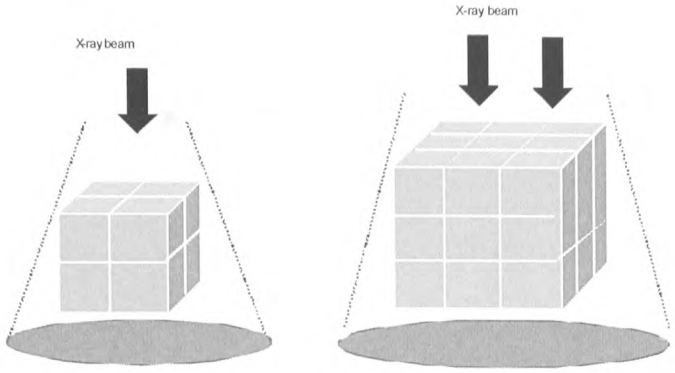
Mathematically, the intensity of the incident x-rays for low (I_{0L}) and high (I_{0H}) energies are reduced exponentially after passing through bone (B) and soft tissue (S) according to the following equations:

$$I_L = I_{0L} \exp -(\mu_{SL} M_S + \mu_{BL} M_B) \qquad \textbf{Equation A1.4}$$

$$I_H = I_{0H} \exp -(\mu_{SH} M_S + \mu_{BH} M_B) \qquad \textbf{Equation A1.5}$$

Where : μ is the mass attenuation coefficient of the material
M is the mass per unit area

DXA provides a bone mineral density (BMD) measurement based on a two-dimensional projection of a three-dimensional structure. Bone mineral content is assessed from a single projection and adjusted for bone area to give an areal density in gcm^{-2}. One source of error is therefore bone size which is especially important if using DXA in children (Figure 1.10).



Mineral Weight	16	54
Volume (cm^3)	8	27
Projected area (cm2)	4	9
Volumetric BMD (gcm^{-3})	2	2
Areal BMD (gcm^{-2})	4	6

Figure A1.10 Illustration of size effect of areal BMD
(from A Practical Guide to Bone Densitometry in Children, NOS 2004)

Attempts to correct this error by using dimensions of bone from a lateral projection improve facture risk prediction at the spine[77] but not at hip of forearm[78 79].

2.6 Calibration

The system is calibrated to give bone mineral density (BMD) in gcm^{-2} using bone and tissue standards of known density. These are either embedded in a calibration block (GE-Lunar) or may be fitted within the x-ray tube housing (Hologic) (Figure A1.11).

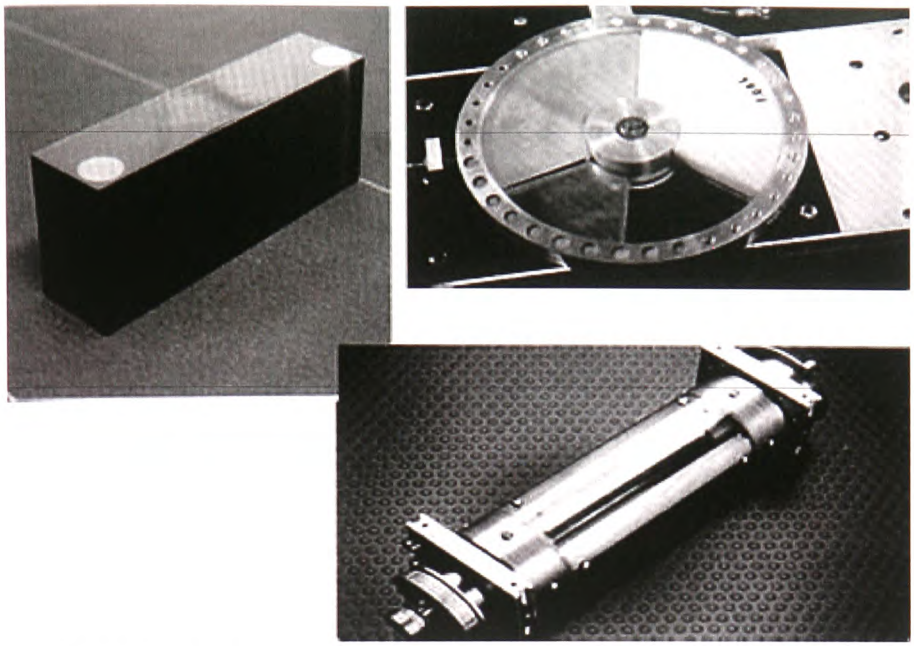


Figure A1.11 Calibration devices for DXA systems: a) GE-Lunar external block, b) Hologic internal wheel, c) Hologic internal drum

Initial factory and on-site calibration during installation is performed to ensure accuracy against factory standards. The systems then require a simple daily calibration procedure to be carried out prior to patient scanning to enable software adjustment to accommodate minor deviations due to changes in environmental conditions.

2.7 DXA Digital Storage

The evolution of the personal computer (PC) during the 1980's provided more rapid processing and improved software applications for manipulation of digital clinical images. This enabled storage and display of images of a resolution sufficient to identify anatomical features and analysis at a speed compatible with clinical applications. The PCs at the time, such as the IBM PS/2 using Intel 8086 16-bit microprocessors, were adequate for handling the scan speeds and resolution of the original pencil beam DXA systems introduced in the late 1980's. Improvements in DXA scanner hardware providing rapid scan times and improved image resolution were mirrored by further improvements in computer hardware and software. During the early days of DXA, scan times were typically 15 minutes and processing time about 3 minutes. Modern systems have scan times 20 to 30 seconds and processing times in seconds despite the much improved resolution and larger image file sizes. Many DXA installations also

now utilise computer networking to enable a second 'workstation' PC to be used for analysis and results printing. Some are linked to the main hospital network for transfer of patient biographic details to populate the scanner patient details file and for transmission of electronic scan reports.

2.8 DXA Technique

The standard anatomical sites used for determination of BMD by DXA are the lumbar spine and the hip. These are accessible in terms of having no overlying bone structures and are important sites for determining bone strength associated with osteoporosis. The images produced are a pixel by pixel map of BMD (Figure A1.12).

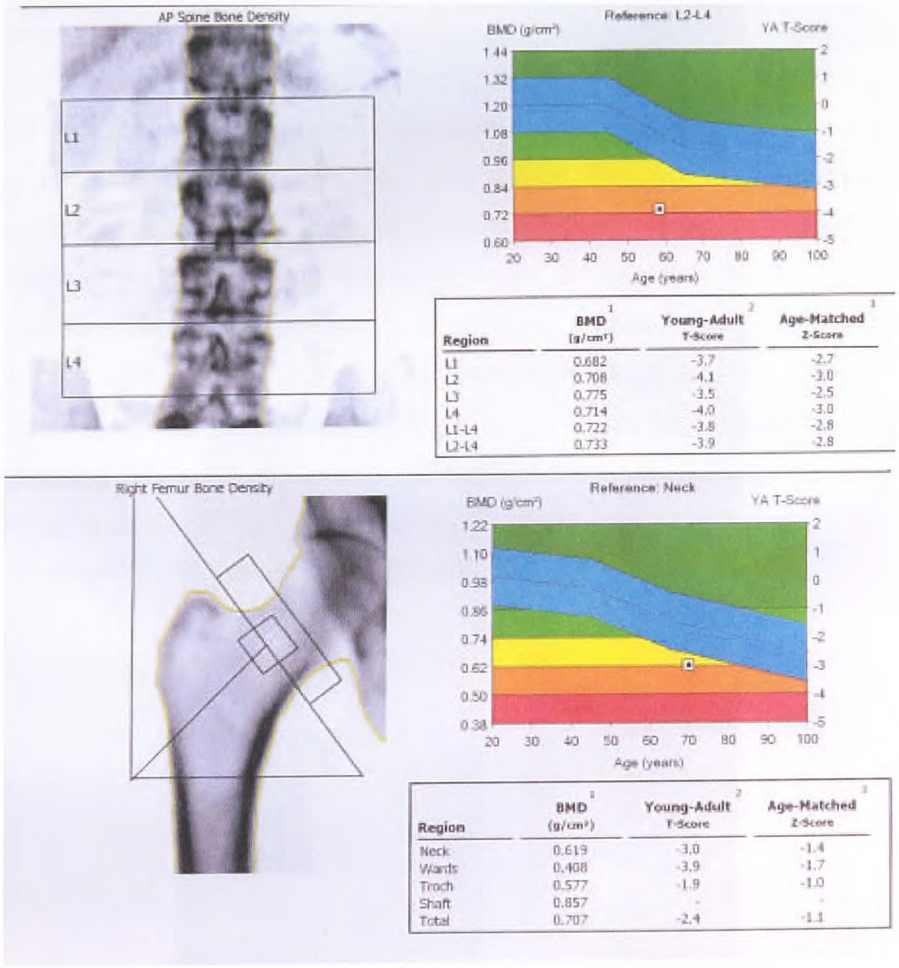


Figure A1.12 DXA images of lumbar spine and femoral neck and associated results produced by a Lunar Prodigy system

The DXA software identifies each pixel as composing primarily bone or soft tissue based on the differential attenuation of the 2 x-ray energies. Where this is

uncertain due to partial volume effect around the edges of the bone, the pixels are 'typed' as neutral and any high attenuating materials such as metal components are 'typed' as being an artefact. Only the 'bone' and soft tissue areas are used in the determination of BMD. The regions of interest shown by the black lines on the scan images in figure A1.12 are placed automatically but are adjustable by the operator when required.

2.9 Quality Assurance

DXA provides a quantitative measure of BMD that is used directly in decision making over clinical management. It is therefore essential that this value is accurate and that any changes observed during longitudinal follow-up represent real changes in BMD. Because of the steep gradient of the relationship between BMD and fracture risk, with a doubling of risk for every one standard deviation change[4] the degree of precision required of these systems is higher than that for many other technologies associated with clinical diagnosis. Optimal results are obtained by use of well trained operators, good technique, reliable, well maintained equipment and adherence to a rigorous quality assurance programme. The daily calibration procedures include checks on scan arm movement, x-ray output and detector sensitivity and discrimination. Following the calibration, an independent scan is recommended using a phantom representing the lumbar spine to confirm that any variation in BMD remains within acceptable limits. Appropriate phantoms are provided with the DXA scanners by the manufacturers (Figure A1.13).

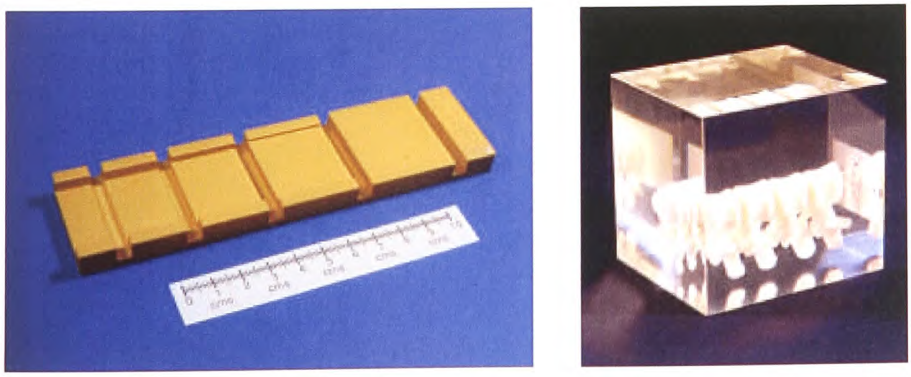


Figure A1.13 Examples of spine phantoms provided with Lunar (left) and Hologic (right) DXA scanners

Reliability of results can also be compromised by patient related factors. Excessive tissue volumes within the scan region due to obesity increase the attenuation of x-rays, particularly those of low energy, leading to decreased counting statistics and inaccuracies due to a shift in spectral distribution to higher effective photon energies (beam hardening). Reduced tissue volumes may also lead to inaccuracies due to too many x-rays reaching the detector leading to detector saturation. Alternative scan modes are usually provided to minimise these errors. The presence of external or internal artefacts or anatomical abnormalities such as fractures may affect determination of BMD and these should be removed where possible or excluded from the areas used in the calculation. The scan image displayed on the computer is used to check accuracy of patient positioning and presence of artefacts and abnormalities.

APPENDIX II

OSTEOPOROSIS

1 Bone structure

Bone is composed of an outer cortical shell and inner trabecullar bone, with the proportions varying by site. Bone is constantly being replenished by a cyclical process involving osteoclasts (bone absorbers) and osteoblasts (bone builders) which ensures good bone health and ability to withstand normal stresses and strains (A2.1).

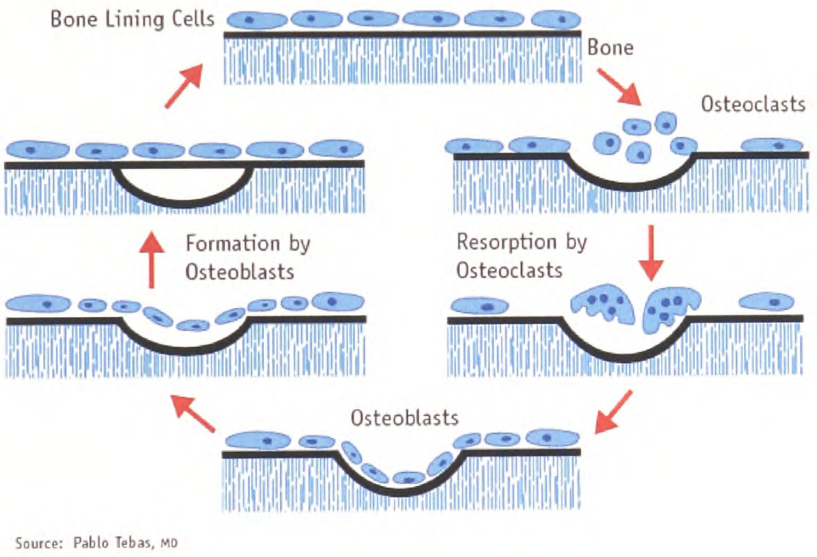
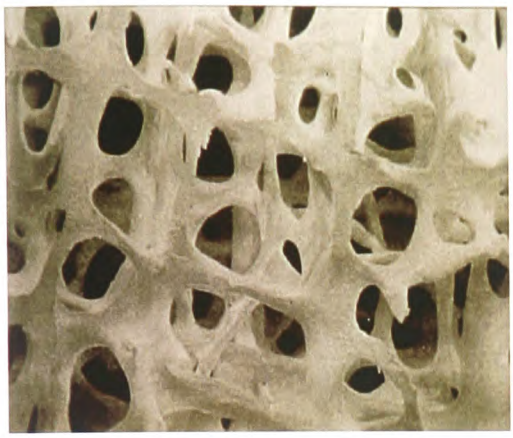


Figure A2.1 Diagram of bone turnover cycle

This metabolic activity occurs on the surface of bone and hence is greater in trabecullar bone which has a larger surface to volume ratio. When these processes are in balance there is preservation of bone but if the balance is disturbed, such as during the menopause, there may be a net loss of bone mass at the end of the cycle. This eventually results in thinning of the bone structure and loss of trabecullar connectivity (Figure A2.2), weakening the bone's ability to withstand the stresses of normal activity and increasing the risk of fracture.

a



b

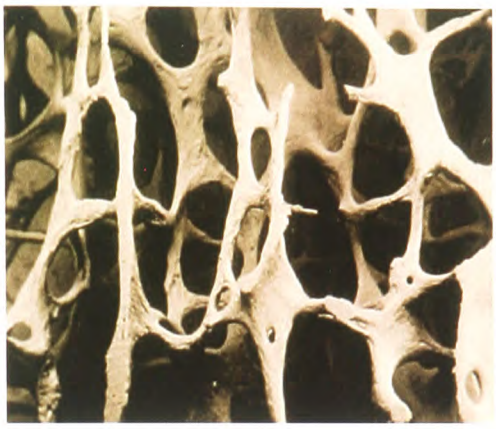
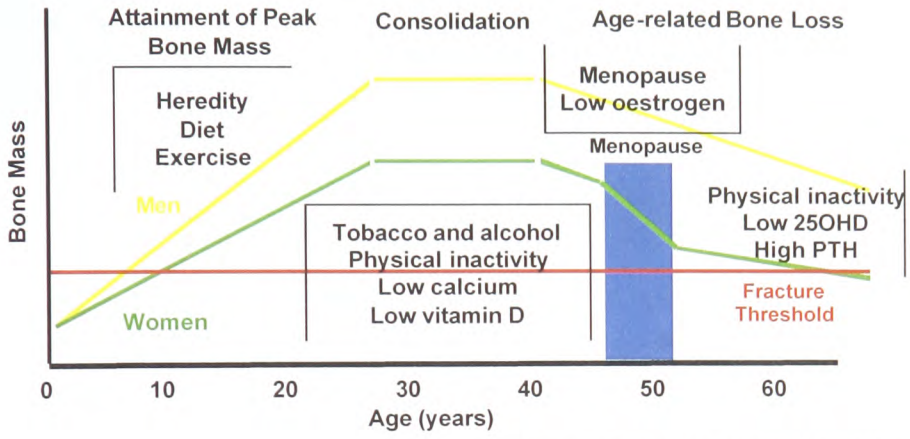


Figure A2.2 Magnified images of trabecullar bone structure: a) normal and b) osteoporotic

In the normal skeleton around 75% of the bone volume is bone marrow and fat, the proportions varying by site and age. These components have different x-ray attenuating properties at the energies used in DXA. Consequently, an excess of yellow (fatty) marrow as seen with aging can give a falsely low BMD.

2 Changes in bone mass with age

Bone mass increases with age until a peak is achieved around 25 years of age. There is then a plateau during adulthood with an age related decline commencing around 45 years which is compounded in women by the menopause related loss[80] [81]. The loss of oestrogen at this stage leads to an increase in osteoclast numbers with consequent larger than normal resorption cavities which are incompletely filled. Factors mediate bone development, maintenance and decline, some of which are modifiable lifestyle factors but some are not (Figure A2.3).



Compston JE. Clin Endocrinol 1990; 33:653–682.

Figure A2.3 Age related changes in bone mass and factors influencing bone status.

As bone mass declines so fractures increase in both women and men (Figure A2.4). The most common sites of fragility fracture are the spine, wrist and hip[82].

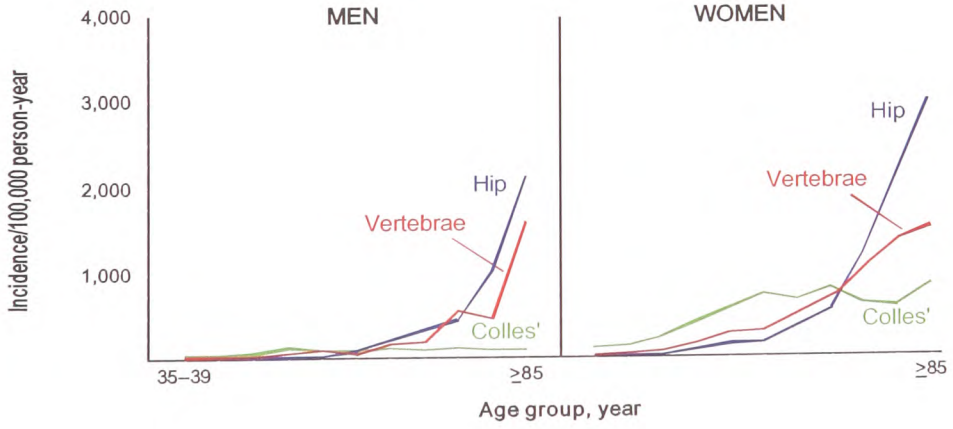


Figure A2.4 Sites of fracture (from *Cooper C. Epidemiology of Osteoporosis. Chapter 49:IV. Metabolic Bone Diseases. Am Soc for Bone & Min Research 2003*)

3 Definition of Osteoporosis

In 1994, a quantitative measure of bone strength was chosen by the WHO to provide a definition of osteoporosis[83]. The definition is based on DXA of the spine, hip and forearm and is applicable only to postmenopausal women (Figure A2.5).

BMD T-SCORE	DIAGNOSIS
> -1	NORMAL
< -1, > -2.5	OSTEOPENIA
< - 2.5	OSTEOPOROSIS
< - 2.5 PLUS FRAGILITY FRACTURE	SEVERE OSTEOPOROSIS

Figure A2.5 World Health Organistion (WHO) quantitaive definition of osteoporosis: based on T-score by DXA (number of standard deviations from young normal mean).

Osteoporosis is defined as a skeletal disease characterised by low bone mass and microarchitectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture[84]. It is a prevalent disease affecting 1 in 2 women and 1 in 5 men[85] and is a major drain on healthcare resources due to the high burden of morbidity and mortality associated with low trauma fractures[86]. Hip fracture in particular often leads to loss of independence with a consequent strain on social services and has a 25% mortality rate within one year[82 87]. Osteoporosis affects primarily females as they reach a lower peak bone mass and suffer oestrogen deficiency related bone loss following the menopause.

4 Other Risk Factors for Fracture

The definition of osteoporosis by BMD was never meant to be used as a treatment threshold in individuals. It is estimated that 70% of the variability in bone strength is determined by bone mass but there are other factors in addition to BMD that are associated with bone strength and fracture risk. These include

age, propensity to fall and bone geometry (Faulkner 1993). It is also known that steroid use or prior fragility fracture is associated with increased risk of future fracture independent of BMD. These factors should be taken into consideration in individual patient management.

5 Bone protective treatments

Over the last 25 years, pharmaceuticals have been developed with bone protective properties and effectiveness in preventing fragility fractures (Figure A2.6).

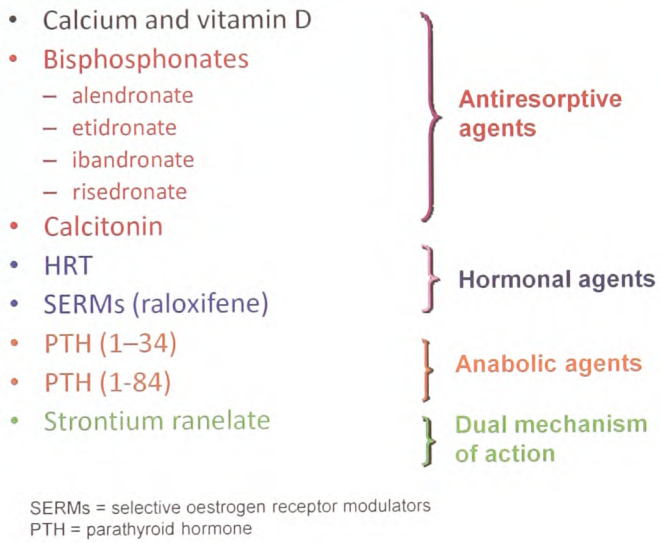


Figure A2.6 Treatments available for protection against bone loss

These developments went hand-in-hand with the introduction of DXA which identified those at high risk of fragility fracture who may benefit from bone protective treatment.

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STANDARDS IN CLINICAL DUAL ENERGY X-RAY ABSORPTIOMETRY

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Submission for PhD: November 2009

Publications

APPENDIX III: Equipment Evaluation and Quality Assurance

Paper 1 An assessment of the radiation dose to patients and staff from a Lunar Expert-XL fan beam densitometer. Steel SA, Baker AJ, Saunderson JR. Physiol. Meas.1998 19:17-26

Paper 2 Image Resolution of the Lunar Expert-XL. Thorpe J, Steel SA. Osteoporosis Int 1999 10(2):95-101

Paper 3 A phantom for evaluating bone mineral density of the hand by dual energy x-ray absorptiometry. Steel SA, Swann P Langley G and Langton CM. Physiol Meas. 1997 18: 233-240

Paper 4 Development and Evaluation of a phantom for morphometric x-ray absorptiometry. Steel SA, Thorpe JA, Walker R, Howey S, Langton CM. Osteoporosis Int 1999, 9(1):38-44

Paper 5 A phantom based study on the effect of subject positioning on morphometric x-ray absorptiometry using the Lunar Expert-XL. Thorpe JA, Steel SA, Langton CM. Br J Radiol. 1998, 71(851):1153-1161

Paper 6 The DXL Calscan Heel Densitometer: Evaluation and Diagnostic Thresholds. Thorpe JA, Steel SA. Br J Radiol. 2006, 79(940):336 – 341

Paper 7 The Alara Metriscan Phalangeal Densitometer: Evaluation and Triage Thresholds. Thorpe JA, Steel SA. Br J Radiol. 2008, 81(970):778-83

APPENDIX IV: Clinical application

Paper 8 The technical and logistical feasibility of population densitometry using DXA and directed HRT intervention: a 2 year prospective study. Purdie DW, Steel SA, Howey S, Doherty SM. Osteoporosis Int. 1996, Suppl. 3:S31-S36

Paper 9 Coeliac disease and bone mineral density in adult female patients. Pistorius LR, Wseidan WH, Purdie DW, Steel SA, Howey S, Bennett JR, Sutton DR. Gut 1995 37(5):639-642.

Paper 10 Factors affecting long-term adherence to hormone replacement therapy after screening for osteoporosis. Steel SA, Albertazzi P, Howarth EM, Purdie DW. Climacteric 2003; 6(2):96-103

Paper 11 The effects of short term Hormone Replacement Therapy on long term bone mineral density (Short term HRT and BMD). Middleton E T, Steel S A. Climacteric 2007;10 (3):257-263

Paper 12 Routine versus targeted vertebral fracture assessment for the detection of vertebral fractures. Middleton E T, Steel S A. Osteoporosis Int. 2008 19(8):1167-73

APPENDIX V: Raising of standards through education and guidance

National Osteoporosis Society National Bone Densitometry Training Scheme literature.

Data Management and Report Generation. Steel S A. In: Fundamentals of Bone Densitometry. (publication prepared by working party of NOS Scientific Advisory Committee - Chair: Professor Francis Ring). Publishers: National Osteoporosis Society, 2006.

The Bone Densitometry Service. Steel S A. In: Fundamentals of Bone Densitometry. (publication prepared by working party of NOS Scientific Advisory Committee - Chair: Professor Francis Ring). Publishers: National Osteoporosis Society, 2006.

Guidelines for the provision of a clinical bone densitometry service. Steel S A, McCrea J D, Ryan PJ. Publishers: National Osteoporosis Society May 2002

Position statement on the reporting of dual energy X-ray absorptiometry (DXA) bone mineral density scans. Fogelman I, Adams J, McCrea J, Steel S A, Blake G M. Publishers: National Osteoporosis Society. August 2002

PUBLICATIONS

ich	Authors as listed, title of publication, publication reference	Refereed (Y/N)	ISSN	
	EQUIPMENT EVALUATION AND QUALITY ASSURANCE			
	Steel SA, Baker AJ, Saunderson JR. An assessment of the radiation dose to patients and staff from a Lunar Expert-XL fan beam densitometer. Physiol. Meas. 19 (1998) 17-26	Y		
	Thorpe J, Steel SA. Image Resolution of the Lunar Expert-XL. Osteoporosis Int 1999 10:95-101	Y		
	Steel SA, Swann P Langley G and Langton CM. A phantom for evaluating bone mineral density of the hand by dual energy x-ray absorptiometry. Physiol Meas. 1997 18:233-240	Y		
	Steel SA, Thorpe JA, Walker R, Howey S, Langton CM. Development and Evaluation of a phantom for morphometric x-ray absorptiometry. Osteoporosis Int 1999, 9:38-44	Y		

	Thorpe JA, Steel SA, Langton CM. A phantom based study on the effect of subject positioning on morphometric x-ray absorptiometry using the Lunar Expert-XL. BJRadiol. 1998 1153-1161. **NOS Young Investigator Award for JT**	Y		
	Thorpe JA, Steel SA. The DXL Calscan Heel Densitometer: Evaluation and Diagnostic Thresholds. British Journal of Radiology – 79 (2006), 336 – 341	Y		
	Thorpe JA, Steel SA. The Alara Metriscan Phalangeal Densitometer: Evaluation and Triage Thresholds. British Journal of Radiology. Br J Radiol. 2008, 81(970):778-83	Y		
	Steel SA, Goodby A, Smith A, Howey S. Long Term (7 years) precision and correlation of three Lunar DXA machines.12th Int Bone Densitometry Workshop, Crieff, Scotland. 18-22 May 1997	Y		
	Goodby A, Steel SA. Factors affecting accuracy of bone mineral density measurement using a Lunar Expert-XL fan beam densitometer. Bone Densitometry Workshop, Warnemunde, Germany. 3-8 Sept 2000	Y		

	Steel SA, Redmond M, Thorpe JA, Howey S. .An assessment of in-vivo precision of AP spine bone densitometry using a Lunar Expert-XL fan beam densitometer. 13th International Bone Densitometry Workshop. 4-8 October 1998, Wisconsin, USA	Y		
	S A Steel, A Goodby, J Saunderson. The GE-Lunar Prodigy: in-vitro precision, cross calibration and radiation dose.15th International Bone Densitometry Workshop. 21-26 July 02 Monterey	y		
	Steel S A. The GE-Lunar Prodigy: in-vivo precision and cross calibration 15th International Bone Densitometry Workshop. July 02. Monterey, California	y		
	Steel SA, Howey S. Diagnostic thresholds for peripheral DXA and BUA. VI Annual Scientific Meeting - ISCD, Rio de Janeiro. 8-13th May 2000 **ISCD Best Poster Award**	Y		

PAPERS		CLINICAL APPLICATION					
8	1990-96	Purdie DW, Steel SA, Howey S, Doherty SM. The technical and logistical feasibility of population densitometry using DXA and directed HRT intervention: a 2 year prospective study. Osteoporosis Int. (1996) Suppl. 3:S31-S36	Y		6	1996	50%
9	1993-95	Pistorius LR, Wseidan WH, Purdie DW, Steel SA, Howey S, Bennett JR, Sutton DR. Coeliac disease and bone mineral density in adult female patients. Gut 1995 37:639-642.	Y		4	1995	35%
10	2002-03	Steel SA, Albertazzi P, Howarth EM, Purdie DW. Factors affecting long-term adherence to hormone replacement therapy after screening for osteoporosis. Climacteric 2003;6:96-103	Y		8	2003	60%
11	2006-07	Middleton E T, Steel S A. The effects of short term Hormone Replacement Therapy on long term bone mineral density (Short term HRT and BMD). Climacteric 2007 10 (3):257-263	Y		7	2007	50%
12	2007-08	Middleton E T, Steel S A. Routine versus targeted vertebral fracture assessment for the detection of vertebral fractures.. Osteoporosis International. Osteoporosis Int. 2008 19(8):1167-73	Y	*0937-941X*	7	2008	50%

ABSTRACTS							
7	1990-97	Steel SA, Purdie DW, Howey S. A 5 year prospective study of BMD behaviour in perimenopausal women. ASBMR-IBMS Second Joint Meeting 1-6 December 1998, San Francisco	Y		11	1998	70%

		RAISING OF STANDARDS THROUGH EDUCATION AND GUIDANCE					
	2002-09	National Training Scheme for Bone Densitometry: • Registration Form • Scheme Rules and Regulations • Syllabus • Programme • Application for Certification • Portfolio requirements • Certification admission appeal	Y*		18	2002 +revisions	40%
	2005-06	S A Steel. The Bone Densitometry Service. In: Fundamentals of Bone Densitometry: 2nd edition (publication prepared by working party of NOS Scientific Advisory Committee - Chair: Professor Francis Ring). Publishers: National Osteoporosis Society 2006: Chapter 7	Y**		5	2006	100%

	2005-06	Steel S A. Data Management and Report Generation. In: Fundamentals of Bone Densitometry: 2nd edition (publication prepared by working party of NOS Scientific Advisory Committee - Chair: Professor Francis Ring). Publishers: National Osteoporosis Society, 2006: Chapter 6	Y**		6	2006	100%
	2001-02	Guidelines for the provision of a clinical bone densitometry service. Steel S A, McCrea J D, Ryan PJ. Publishers: National Osteoporosis Society May 2002	Y*		7	2002	40%
	2001-02	Position statement on the reporting of dual energy X-ray absorptiometry (DXA) bone mineral density scans. Fogelman I, Adams J, McCrea J, Steel S A, Blake G M. Publishers: National Osteoporosis Society. August 2002	Y*		13	2002	20%

Y* Reviewed and approved by Medical Board of the National Osteoporosis Society
Y** Course material reviewed and the course accredited by 2 Professional Bodies: the Institute of Physics and Engineering in Medicine and the College of Radiographers.

Statements of Support

confirm the following contributions from Ms S A Steel to the publications below:

Publication	Contribution	Percent
Steel SA, Swann P Langley G and Langton CM. A phantom for evaluating bone mineral density of the hand by dual energy x-ray absorptiometry. Physiol Meas. 18(1997) 233-240	• Concept and design of the study • Design of the hand phantom • Supervision of production of phantom • Established protocols and procedures for conduct of study • Designed and maintained database of results • Responsible for quality assurance of equipment and measurements • Performed the measurements • Responsible for analysis of data • Main author of the paper • Contributed most of references	70%
Steel SA, Thorpe JA, Walker R, Howey S, Langton CM. Development and Evaluation of a phantom for morphometric x-ray absorptiometry. Osteoporosis Int 1999, 9:38-44	• Concept and design of the study • Design of the phantom • Supervision of production of phantom • Established protocols and procedures for conduct of study • Designed and maintained database of results • Responsible for quality assurance of equipment and measurements • Performed the measurements • Responsible for analysis of data • Main author of the paper • Contributed most of references	60%
Thorpe JA, Steel SA, Langton CM. A phantom based study on the effect of subject positioning on morphometric x-ray absorptiometry using the Lunar Expert-XL. BJRadiol. 1998 1153-1161.	• Concept and design of the study • Design of the phantom • Supervision of production of phantom • Established protocols and procedures for conduct of study • Designed and maintained database of results • Responsible for quality assurance of equipment and measurements • Supervised the measurements • Responsible for analysis of data • Co-author of the paper • Contributed most of references	45%

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Statements of Support

I confirm the following contributions from Ms S A Steel to the publications below:

Publication	Contribution	Percent
National Osteoporosis Society National Bone Densitometry Training Scheme literature.	• Contributed to development of training scheme • Contributed to contents of Syllabus, and Rules and Regulations, • Produced slides and deliver lectures on *Standards for a Hospital Based Bone Densitometry Service* and *Principles of DXA.* • Set examination questions for the on-line exam • Designed marking scheme and scoresheet for marking of portfolios.	40%

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I confirm the following contributions from Ms S A Steel to the publications below:

Publication	Contribution	Percent
Steel S A, McCrea J D, Ryan PJ. Guidelines for the provision of a clinical bone densitometry service. Publishers: National Osteoporosis Society May 2002	• Main author of document	60%

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Statements of Support

I confirm the following contributions from Ms S A Steel to the publications below:

Publication	Contribution	Percent
Steel SA, Albertazzi P, Howarth EM, Purdie DW. Factors affecting long-term adherence to hormone replacement therapy after screening for osteoporosis. Climacteric - 2003;6:96-103	• Contributed to design of the study • Established protocols and procedures for conduct of study • Designed and maintained database of results • Responsible for quality assurance of equipment and measurements • Supervision of the measurements • Contributed to analysis of data • Main author of the paper • Contributed to references	50%

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Statements of Support

I confirm the following contributions from Ms S A Steel to the publications below:

Publication	Contribution	Percent
Goodby A, Steel SA. Factors affecting accuracy of bone mineral density measurement using a Lunar Expert-XL fan beam densitometer. Bone Densitometry Workshop, Warnemunde, Germany. 3-8 Sept 2000	• Concept of the study • Supervision of the study as part of MSc supervision • Responsible for quality assurance of equipment and measurements • Co-author of the poster	30%
S A Steel, A Goodby, J Saunderson. The GE-Lunar Prodigy: in-vitro precision, cross calibration and radiation dose. 15th International Bone Densitometry Workshop. 21-26 July 02 Monterey	• Concept and design of the study • Established protocols and procedures for conduct of study • Designed and maintained database of results • Responsible for quality assurance of equipment and measurements • Supervised and performed some of the measurements • Responsible for analysis of data • Main author of the poster	60%

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21st June 2008

Statements of Support

I confirm the following contributions from Ms S A Steel to the publications below:

Publication	Contribution	Percent
Middleton E T, Steel S A. The effects of short term Hormone Replacement Therapy on long term bone mineral density (Short term HRT and BMD). Climacteric – 2007;10 (3):257-263	• Contributed to design of the study • Established protocols and procedures for conduct of study • Designed and maintained database of results • Responsible for quality assurance of equipment and measurements • Supervision of the measurements • Analysis of data • Joint author of the paper • Contributed to references	50%
Middleton E T, Steel S A. Routine versus targeted vertebral fracture assessment for the detection of vertebral fractures. Osteoporosis International – In Press	• Contributed to design of the study • Established protocols and procedures for conduct of study • Designed and maintained database of results • Responsible for quality assurance of equipment and measurements • Supervision of the measurements • Analysis of data • Joint author of the paper • Contributed to references	50%

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Statements of Support

I confirm the following contributions from Ms S A Steel to the publications below:

Publication	Contribution	Percent
Fogelman I, Adams J, McCrea J, Steel S A, Blake G M. Position statement on the reporting of dual energy X-ray absorptiometry (DXA) bone mineral density scans. Publishers: National Osteoporosis Society. August 2002	• Contributed to writing of document • Contributed DXA images used in document	20%

Agreed by Ignac Fogelman

Prof I Fogelman
King's College, London

21st June 2008

Statements of Support

I confirm the following contributions from Ms S A Steel to the publications below:

Publication	Contribution	Percent
Steel SA, Baker AJ, Saunderson JR. An assessment of the radiation dose to patients and staff from a Lunar Expert-XL fan beam densitometer. Physiol. Meas. 19 (1998) 17-26	• Concept and design of the study • Designed and maintained database of results • Responsible for quality assurance of equipment • Performed the measurements • Contributed to analysis of data • Main author of the paper • Contributed most of references	70%

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Statements of Support

I confirm the following contributions from Ms S A Steel to the publications below:

Publication	Contribution	Percent
Purdie DW, Steel SA, Howey S, Doherty SM. The technical and logistical feasibility of population densitometry using DXA and directed HRT intervention: a 2 year prospective study. Osteoporosis Int. (1996) Suppl. 3:S31-S36	• Contributed to design of the study • Established protocols and procedures for conduct of study • Designed and maintained database of results • Responsible for quality assurance of equipment and measurements • Supervision of the measurements • Responsible for analysis of data • Co-author of the paper • Contributed to references	50%
Hamed HM, Purdie DW, Steel SA, Howey S. The relation between bone mineral density and early pregnancy loss. British Journal of Obs and Gynae. (1992) Vol 99:946-949	• Contributed to design of the study • Established protocols and procedures for conduct of study • Designed and maintained database of results • Responsible for quality assurance of equipment and measurements • Supervision of the measurements • Responsible for analysis of data • Co-author of the paper • Contributed to references	40%
Hamed HM, Purdie DW, Ramsden CS, Carmichael B, Steel SA, Howey S. Influence of Birth weight on adult bone mineral density. British Journal of Obs and Gynae. (1992) Vol99: 946-949	• Contributed to design of the study • Established protocols and procedures for conduct of study • Designed and maintained database of results • Responsible for quality assurance of equipment and measurements • Supervision of the measurements • Responsible for analysis of data • Co-author of the paper • Contributed to references	40%
Pistorius LR, Wseidan WH, Purdie DW, Steel SA, Howey S, Bennett JR, Sutton DR. Coeliac disease and bone mineral density in adult female	• Contributed to design of the study • Established protocols and procedures for conduct of study • Designed and maintained	35%

patients. Gut (1995) 37:639-642.	database of results • Responsible for quality assurance of equipment and measurements • Supervision of the measurements • Responsible for analysis of data • Co-author of the paper • Contributed to references	
Steel SA, Goodby A, Smith A, Howey S. Long Term (7 years) precision and correlation of three Lunar DXA machines. 12th Int Bone Densitometry Workshop, Crieff, Scotland. 18-22 May 1997	• Concept and design of the study • Established protocols and procedures for conduct of study • Designed and maintained database of results • Responsible for quality assurance of equipment and measurements • Supervision of the measurements • Responsible for analysis of data • Main author of the poster	60%
Steel SA, Redmond M, Thorpe JA, Howey S. An assessment of in-vivo precision of AP spine bone densitometry using a Lunar Expert-XL fan beam densitometer. 13th International Bone Densitometry Workshop. 4-8 October 1998, Wisconsin, USA	• Concept and design of the study • As Principal Investigator, obtained ethics approval • Established protocols and procedures for conduct of study • Designed and maintained database of results • Responsible for quality assurance of equipment and measurements • Supervision of the measurements • Responsible for analysis of data • Main author of the poster	60%
Steel SA, Howey S. Diagnostic thresholds for peripheral DXA and BUA. VI Annual Scientific Meeting - ISCD, Rio de Janeiro. 8-13th May 2000	• Concept and design of the study • As Principal Investigator, obtained ethics approval • Established protocols and procedures for conduct of study • Designed and maintained database of results • Responsible for quality assurance of equipment and measurements • Supervision of the measurements • Responsible for analysis of data • Main author of the poster	70%
Steel SA, Purdie DW, Howey S. A 5 year prospective study of BMD behaviour in perimenopausal women. ASBMR-IBMS Second Joint Meeting 1-6 December 1998, San Francisco	• Concept and design of the study • Established protocols and procedures for conduct of study • Designed and maintained database of results • Responsible for quality assurance of equipment and measurements • Supervision of the measurements	70%

	• Responsible for analysis of data • Main author of the poster	

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21st June 2008

Statements of Support

I confirm the following contributions from Ms S A Steel to the publications below:

Publication	Contribution	Percent
Thorpe J, Steel SA. Image Resolution of the Lunar Expert-XL. Osteoporosis Int 1999 10:95-101	• Concept and design of the study • supervision of the measurements • joint author of the paper • contributed half of references	50%
Thorpe JA, Steel SA. The DXL Calscan Heel Densitometer: Evaluation and Diagnostic Thresholds. British Journal of Radiology – 79 (2006), 336 – 341	• Concept and design of the study • as Principal Investigator obtained ethical approval • supervision of the measurements • joint author of the paper • contributed half of references	50%
Thorpe JA, Steel SA. The Alara Metriscan Phalangeal Densitometer: Evaluation and Triage Thresholds. BJR – In Press	• Concept and design of the study • as Principal Investigator obtained ethical approval • supervision of the measurements • joint author of the paper • contributed half of references	50%

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21st June 2008

APPENDIX III

Equipment Evaluation and Quality Assurance

(Papers 1 to 7)

Physiol. Meas. 19 (1998) 17–26. Printed in the UK PII: S0967-3334(98)86730-0

An assessment of the radiation dose to patients and staff from a Lunar Expert-XL fan beam densitometer

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Abstract. Dual-energy x-ray absorptiometry (DXA) is a widely used technique for measuring bone mineral density for the identification and management of osteoporotic subjects. The original DXA pencil beam systems expose patients to an effective dose of ionizing radiation of around 2 μSv and require no additional protective shielding for staff. The new fan beam densitometers incorporate solid state detectors and have a higher photon flux, enabling faster acquisition times and giving improved resolution. However, this may be at the expense of higher radiation dose. This study was conducted to assess the radiation dose to patients and staff from the standard scan modes using a Lunar Expert-XL fan beam densitometer. This is, we believe, the first dose assessment of the Expert-XL. The results indicate that the scatter dose at 1 m from the scan table, assuming four AP spine and femoral neck examinations per hour, is about 4 μSv h^{-1}. This is well below the limit of 7.5 μSv h^{-1} set by the UK's Ionising Radiation Regulations for defining a Controlled Area but above the lesser limit of 2.5 μSv h^{-1} for a Supervised Area. Typical effective doses to patients are 59 μSv for an AP lumbar spine scan, up to 56 μSv for AP femoral neck, 71 μSv for lateral spine morphometry and 75 μSv for whole body. Although exceeding those of pencil beam DXA machines, these doses are less than for standard radiographic procedures, particularly of the lumbar spine. Where reduced scan time, improved image resolution or morphometric analysis of the spine are required, the patient doses from the Lunar Expert-XL are not prohibitive.

Keywords: DXA, dosimetry, fan beam, BMD

1. Introduction

Dual-energy x-ray absorptiometry (DXA) is an accurate, precise and widely used technique for measuring bone density to identify and monitor osteoporotic subjects and to assess the effectiveness of treatment. The original DXA systems use a pencil beam x-ray and a sodium iodide scintillation detector moving, in unison, in a rectilinear fashion over the region of interest. With the advent of new fan beam densitometers, incorporating solid state detectors, faster acquisition times and improved resolution is made possible, although possibly at the expense of higher radiation dose. The Ionising Radiation Regulations (IRR 1985) and Approved Codes of Practice (ACOP 1985) aim to maintain radiation doses 'as low as reasonably achievable' (the ALARA principle). In order to comply with these regulations an assessment of the risk to staff and patients is required.

The quantity used to assess radiation hazard is the effective dose, which is the sum of the absorbed doses to each irradiated organ, weighted for the radiation type and radiosensitivity of the organ. The intention of this weighting process is to produce a value that is proportional

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to the risk of inducing cancer or hereditary disease. This study was conducted to assess the effective dose from a Lunar Expert-XL fan beam densitometer (Lunar Corp., Madison, WI, USA).

Such an assessment has been performed by others (Njeh *et al* 1996). However, this work was performed on a prototype machine (the Lunar Expert) using a now obsolete scan mode. Also, no mention is made in the paper about the contribution of scattered radiation to organs outside the primary beam.

2. Method

2.1. Lunar Expert-XL

The Lunar Expert-XL uses a fan beam of x-rays and an array of solid state scintillation detectors. The x-ray tube operates at a maximum continuous voltage of 134 kV and maximum tube current of 5 mA with 2 mm aluminium filtration. Original DXA systems use either a k-edge filter or kV switching to produce two discrete x-ray energies, of around 40 and 70 keV, chosen to optimize the differential attenuation between bone and soft tissue. The Expert-XL achieves this by dual-energy discrimination at the detector with one row of elements recording the low-energy and one the higher-energy x-rays. The x-ray tube and detector are mounted on a C-arm which may be rotated to enable lateral imaging. The distance from focal spot to image receptor is 112 cm. The system is capable of performing bone densitometry measurement of the lumbar spine, femoral neck, whole body, forearm, hand and morphometric assessment of the thoracic and lumbar vertebrae.

2.2. Rando anthropomorphic phantom

A Rando anthropomorphic phantom (Alderson Research Laboratory, Stamford, CT, USA) was used to determine doses at different depths within the body. The Rando phantom consists of a human skeleton embedded in a soft tissue equivalent material (density 0.985 g cm^{-3}, effective atomic number 7.30). Air-expanded material (density 0.3 g cm^{-3}) is incorporated to represent the lungs. The proportions of the phantom were determined from a survey of United States Air Force personnel, and the overall stature scaled to match the civilian population (height 1.73 m, weight 73.5 kg). It may be considered to represent a standard man as defined by the International Commission on Radiological Protection (ICRP 1975). The phantom is of standard male form, although breast attachments are available and were utilized for this study. The phantom is separated into 35 slices, which have an array of holes into which dosimeters or tissue equivalent pegs may be placed.

2.3. Measurement of half-value layer

The phantom is designed for use with photons generated at applied potentials greater than 70 kV, and doses may be significantly overestimated if used with lower energies (IPSM 53 (Wall *et al* 1988)). The phantom may therefore be inappropriate for use with the pencil beam DXA systems. Also, Shrimpton *et al* (1981) recommend that the phantom only be used with radiation with a half-value layer (HVL) of greater than 2 mm aluminium. To validate its use for the assessment of doses from the Lunar Expert-XL, the HVL of the x-ray beam was measured. A 6 cm^3 thimble ionization chamber (MDH 10X5-6) was placed in the beam path and a lead collimator placed above to minimize contributions from scatter. Measurements were performed using a 5 mA service mode. This allowed exposures to be

made with both the x-ray tube and detector stationary. The exposure was repeated with increasing layers of 99.8% pure aluminium filters until the electrometer reading was half that for the unfiltered beam.

2.4. Measurement of dose to staff

Scatter dose rates were measured, at 1 m horizontal distance from the central axis of the scan table, using an Autoness Szintomat 6134A dose rate meter. The uncertainty in dose rate measurement for this instrument does not exceed 20% at the x-ray energies used. A tank of water (width 23 cm, length 35 cm, depth 20 cm) was placed on the table to simulate the scattering that would occur with a patient *in situ*. A scan mode using the maximum tube current of 5 mA was selected.

2.5. Measurement of patient dose

Patient dose was determined using lithium fluoride thermoluminescent dosimeters (TLDs) embedded in the Rando phantom, for whole body, AP spine, lateral spine and femur scans. For each scan mode, TLDs were placed at positions and depths within the phantom corresponding to those of major organs in the primary beam and also in adjacent areas just outside the primary beam to give an estimate of the contribution to the effective dose made by radiation scattered outside the primary field. The numbers of TLDs used to assess each organ/tissue dose for each scan type are listed in table 1. In order to obtain a satisfactory cumulative dose to the TLDs, 30 scans were performed using each scan mode. However, doses recorded on some TLDs outside the primary beam were still found to be below the dose error of 6 μSv stated by the Medical Physics Service, Lincoln, UK who were responsible for the calibration and reading of the TLDs. These doses were still included in the calculations but contribute little to the effective dose per scan. The above service also specifies a 3% standard deviation error due to TLD to TLD variation and about 2% error in the calibration procedure. The cumulative effective of the above on the final effective doses is estimated at 6%.

Table 1. Number of TLDs used for each scan mode.

	Number of TLDs used for each organ/tissue			
Organ/tissue	Whole body	AP spine	Lat. spine	R. femur
Stomach	3	2	2	—
Colon	2	2	1	2
Lung	6	1	7	—
Bone marrow	5	2	5	1
Bladder	2	2	—	4
Oesophagus	5	2	4	—
Breast	3	—	—	—
Liver	7	7	8	—
Ovary	2	1	—	3
Thyroid	1	—	—	—
Bone surface	5	2	5	1
Skin	10	4	10	4
Remainder	14	5	10	6
Total	65	30	52	21

2.6. Calculation of effective dose

The locations of major organs in the Rando phantom were determined using the drawing of reference man from NRPB-R250 (Jones and Shrimpton 1991). The weighting factors for each organ were taken from ICRP 60 (ICRP 1990, 1991). The effective dose is given by

$$E = \sum_T W_T H_T$$

where H_T is the equivalent dose in the organ or tissue T and W_T is the weighting factor for tissue T.

The calculation of effective dose requires a knowledge of: the proportion of each organ within the primary and scatter fields; the extent of scatter; and the average dose to the organs from primary and scatter fields. The above are dependent on the scan area. For the purposes of this assessment the manufacturers recommended scan widths and lengths for each scan mode were used.

By overlaying a rescaled scan field size on the NRPB drawing, the proportion of each organ or tissue within the primary field was determined.

The proportions of skin, red bone marrow and bone within each slice of the phantom were calculated using factors previously determined by Huda and Sandison (1984). The percentages of red bone marrow and bone in the primary beam were calculated by identifying the slices of the Rando phantom exposed to the primary beam. For the femur scan, the percentage calculated was divided by two as only one hip is scanned.

A similar method to that for bone surfaces and red bone marrow was used to calculate the 'remainder' organs in the scan field. This method, however, assumes a uniform distribution of remainder organs in the body. The average dose to these organs is calculated and a weighting factor of 0.05 applied to calculate the contribution to the effective dose. Any remainder organs receiving a dose of greater than the highest dose to any other organ should be considered separately and a weighting factor of 0.025 applied to that organ and 0.025 to the average of the rest of the remainder organs (ICRP 1990, 1991). Therefore, for AP spine, the doses to the intestines, kidneys, spleen and pancreas were calculated to determine whether separate assessment was required as, in this scan mode, these organs are all within the primary beam.

3. Results

3.1. Half-value layer

The manufacturer specifies that the Lunar Expert-XL has 0.5 mm inherent filtration, an additional 2 mm aluminium added filtration and a half-value layer of greater than 2.5 mm aluminium. Our results indicate that the half-value layer is 5.1(±0.1) mm aluminium.

3.2. Dose to staff

The dose rate at 1 m from the central axis of the table, at scan table height, using the maximum tube current of 5 mA, was 50 μSv h^{-1}. A peak dose rate at 1 m of 120 μSv h^{-1} was measured at about tube height. The dose rate at the operator's chair, 2.25 m from the scan table axis, was 17 μSv h^{-1}.

The UK's Ionising Radiation Regulations (1985) require that, 'a Controlled Area be designated, in most circumstances, where the time averaged dose rate (averaged over an 8 h day) is greater than 7.5 μSv h^{-1}'. Such a dose rate for 8 h a day, five days a week

for 50 working weeks a year would result in a dose of 15 mSv, which is the legal dose limit for unclassified radiation workers. Although the maximum legal limit for unclassified workers is 15 mSv, there is no threshold for risk. Risk is proportional to radiation dose therefore doses must be as low as reasonably achievable (ALARA) or as low as reasonably practicable (ALARP, IRR 1985). From our results, the numbers of scans required that would give time averaged dose rates of 7.5 μSv h^{-1}, at 1 m from the table axis, were calculated for various scan modes (table 2). The anticipated workload is considerably less than the limits indicated in table 2, and therefore it was decided that the Controlled Area could safely be limited to within 1 m of the couch. Assuming four fast mode AP spine and femoral neck examinations per hour (eight scans), the scatter dose at 1 m would be 4 μSv h^{-1}. This exceeds the IRR limit for a Supervised Area but is well within that for a Controlled Area. As an additional precaution, and to conform to the ALARA principle a lead-acrylic screen of 0.5 mm lead equivalence, and height 1.54 m was placed between the operator's chair and the scan table. This screen will attenuate in excess of 95% of the scattered radiation incident upon it.

Table 2. Scatter doses at 1 m from centre of scanning table.

Scan mode	Tube current (mA)	Exposure time (s)	Dose rate at 1 m (μSv h^{-1})	Dose at 1 m (μSv/scan)	Scan limits for 7.5 μSv h^{-1} dose rate (scans/day)
Whole body	1.5	231.3	36	2.31	26
AP spine (fast)	5	16	120	0.53	112
Lat. spine morph.	5	38	120	1.27	47
R. femur (fast)	5	14.4	120	0.48	125

3.3. Effective dose to patients

An isodose line of 50 μSv after 30 scans was used to define the extent of the scattered radiation field to be considered for each scan mode. The percentage of tissues and organs within the primary and scatter fields for each scan mode are shown in table 3. For the whole body scan mode, the organ doses have combined primary and scatter components. Tables 4 to 7 show the calculated organ doses, and how they contribute to the final effective dose per scan. Effective doses per scan are summarized in table 8. The total uncertainty for these dose values is estimated at 6%. The effective doses for other scan modes were derived using the calculated effective dose per mA s (table 9).

4. Discussion

The time averaged maximum scatter dose rate at 1 m from the central axis of the scan table is 4 μSv h^{-1} assuming four patients per hour undergoing 5 mA fast AP spine and femur scans. This exceeds the scatter dose of 1.06 μSv h^{-1} stated by Mazess (1996), but his figures are based on the shorter scan times of 6 s of the recently introduced turbo mode. After correcting for difference in scan times, there remains a significant difference in scatter doses, but it is not clear at which height the latter doses were recorded. The results of this study are similar to those stated by Patel *et al* (1996) of 5 μSv h^{-1} . The difference may

Table 3. Percentage of tissue or organ within primary and scatter field for each scan mode.

	Whole body		AP spine		Lateral spine		Right femur	
Organ	Primary	Scatter	Primary	Scatter	Primary	Scatter	Primary	Scatter
Bladder	100%	0	0	10%	0	10%	26%	74%
Bone surfaces	100%	0	14%	0	23%	0	8%	0
Breast	100%	0	0	0	0	100%	0	0
Colon	100%	0	7%	50%	18%	32%	0	0
Gonads	100%	0	0	100%	0	100%	50%* (0)**	50%* (100%)**
Liver	100%	0	58%	42%	55%	42%	0	0
Lung	100%	0	0	22%	50%	50%	0	0
Oesophagus	100%	0	0	19%	15%	50%	0	0
Pancreas***	—	—	50%	—	—	—	—	—
Red bone marrow	100%	0	24%	0	38%	0	14%	0
Remainder	100%	0	18%	0	30%	0	18%	0
Skin	100%	0	4%	14%	11%	19%	3%	13%
Stomach	100%	0	75%	25%	50%	25%	0	0
Thyroid	100%	0	0	0	0	10%	0	0

Calculations performed assuming one ovary within primary field * and excluded from primary field **.

*** Dose to pancreas in AP spine mode found to be higher than that to other organs, therefore, as stipulated in ICRP 60 (ICRP 1990, 1991), a separate assessment was performed in order to calculate effective dose. This assumed that 50% of organ in primary beam and 0% in scatter region.

Table 4. Organ/tissue doses using AP spine fast scan mode on Lunar Expert-XL.

	Mean dose (μSv/scan)		Total	Weighting	
Organ	Primary	Scatter	dose (H_T)	factor (W_T)	$H_T \times W_T$
Bladder		2	2	0.05	0.1
Bone surfaces	23		23	0.01	0.2
Colon	7	48	55	0.12	6.6
Gonads		16	16	0.2	3.2
Liver	132	7	139	0.05	7.0
Lung		5	5	0.12	0.6
Oesophagus		2	2	0.05	0.1
Pancreas	325		325	0.025	8.1
Red bone marrow	40		40	0.12	4.8
Remainder	36		36	0.025	0.9
Skin	18	2	20	0.01	0.2
Stomach	208	16	224	0.12	26.9
				Effective dose 59 μSv	

be due to the measurements being performed with patients *in situ* for the latter compared with the use of a tank of water as the scattering medium in this study.

With an expected workload of four patients per hour, steps should be taken to reduce the dose to the operator by increasing the operator's distance from the scan table and

Table 5. Organ/tissue doses using right femur fast scan mode on Lunar Expert-XL.

(i) Ovaries in primary field

Organ	Mean dose (μSv/scan)		Total dose (H_T)	Weighting factor (W_T)	$H_T \times W_T$
	Primary	Scatter			
Bladder	18	16	34	0.05	1.7
Bone surfaces	11		11	0.01	0.1
Gonads	247	8	255	0.2	51.0
Red bone marrow	19		19	0.12	2.3
Remainder	11		11	0.05	0.6
Skin	9	1	10	0.01	0.1
				Effective dose 56 μSv	

(ii) Ovaries outside primary field

Organ	Mean dose (μSv/scan)		Total dose (H_T)	Weighting factor (W_T)	$H_T \times W_T$
	Primary	Scatter			
Bladder	18	16	34	0.05	1.7
Bone surfaces	11		11	0.01	0.1
Gonads	0	177	177	0.2	35.4
Red bone marrow	19		19	0.12	2.3
Remainder	11		11	0.05	0.6
Skin	9	1	10	0.01	0.1
				Effective dose 40 μSv	

Table 6. Organ/tissue doses using lateral spine morphometry scan mode on Lunar Expert-XL.

Organ	Mean dose (μSv/scan)		Total dose (H_T)	Weighting factor (W_T)	$H_T \times W_T$
	Primary	Scatter			
Bladder		1	1	0.05	0.1
Bone surfaces	39		39	0.01	0.4
Breast		32	32	0.05	1.6
Colon	12	5	17	0.12	2.0
Gonads		16	16	0.2	3.2
Liver	192	33	225	0.05	11.3
Lung	161	48	209	0.12	25.1
Oesophagus	41	11	52	0.05	2.6
Red bone marrow	65		65	0.12	7.8
Remainder	66		66	0.05	3.3
Skin	44	1	45	0.01	0.5
Stomach	72	32	104	0.12	12.5
Thyroid		1	1	0.05	0.1
				Effective dose 71 μSv	

consideration given to installation of a protective screen. In our centre, operators are positioned behind a protective screen at about 2 m from the scan table. Monthly monitoring of operator doses over a period of 1 year using personal film badge dosimeters, demonstrate doses below the limits of detection, i.e. less than 50 μSv per month (0.6 mSv per year). This is well below the current UK legal limits and also below the latest recommended limits

Table 7. Organ/tissue doses using whole body scan mode on Lunar Expert-XL.

Organ	Mean dose (μSv/scan) Primary	Scatter	Total dose (H_T)	Weighting factor (W_T)	$H_T \times W_T$
Bladder	114	0	114	0.05	5.7
Bone surfaces	39	0	39	0.01	0.4
Breast	133	0	133	0.05	6.7
Colon	73	0	73	0.12	8.8
Gonads	77	0	77	0.2	15.4
Liver	54	0	54	0.05	2.7
Lung	55	0	55	0.12	6.6
Oesophagus	77	0	77	0.05	3.9
Red bone marrow	39	0	39	0.12	4.7
Remainder	72	0	72	0.05	3.6
Skin	115	0	115	0.01	1.2
Stomach	58	0	58	0.12	7.0
Thyroid	166	0	166	0.05	8.3
				Effective dose 75 μSv	

Table 8. Effective doses to patient from standard procedures on Lunar Expert-XL.

Scan mode	Tube current (mA)	Scan time (s)	Field width (cm)	Scan length (cm)	Effective dose per scan (μSv)	Effective dose per mA s (μSv mA^{-1} s^{-1})
AP spine (fast)	5	16	17.3	20	59	0.74
AP right femur (fast)	5	14.4	14.7	18	56* 40**	0.78* 0.56**
Lateral spine morphometry	5	38	14.4	38	71	0.37
Whole body (medium)	1.5	131.3	4 sweeps covering whole body		75	0.38

Calculations performed assuming one ovary within primary field * and excluded from primary field **.

for both radiation workers and the general public which are expected to be implemented in January 2000 (ICRP 60 1990, 1991).

Results from this study suggest that scatter doses are higher than those of 2.4 μSv reported by others (Patel *et al* 1996) for the Hologic QDR 4500. However, the different system specification, geometry (e.g. below-table x-ray tube) and choice of scan technique make a direct comparison complex.

The HVL of the Lunar Expert-XL was found to be 5.1 mm aluminium at a set voltage of 134 kV. This quality of radiation is within recommended guidelines for use with the Alderson Rando anthropomorphic phantom. The total effective dose for an AP and lateral morphometric study of the spine was found to be 130 μSv compared with a typical effective dose of 1230 μSv for a lumbar spine radiological examination involving AP and lateral views (table 10). Although the radiation dose to patients from the Expert-XL exceeds that of the standard pencil beam DXAs more than 100 fold (Spencer *et al* 1994, Njeh *et al* 1996), scan time is reduced and the improved resolution provides additional information. Also, the

Table 9. Effective doses for other scan modes derived from the 'effective dose per mA s'.

Scan mode	Tube current (mA)	Scan time (s)	Field width (cm)	Scan length (cm)	Calculated effective dose (μSv)
AP spine (fast)	2	16	17.3	20	24
AP spine (turbo)	5	8	17.3	20	30
AP spine (turbo)	2	8	17.3	20	12
Femur (fast)	2	14.4	14.7	18	22* (16**)
Femur (turbo)	5	7.2	14.7	18	28* (20**)
Femur (turbo)	2	7.2	14.7	18	11* (8**)
Total body (fast)	1.5	65.6	4 sweeps		38

Calculations performed assuming one ovary within primary field * and excluded from primary field **.

Table 10. Some typical effective doses from common radiographs, calculated using typical entrance surface doses measured for adult patients at a random sample of 20 English hospitals[a] and NRPB Monte Carlo data[b].

Examination	Typical effective dose per film (mSv)
Lumbar spine—AP	0.88
Lumbar spine—lateral	0.35
Lumbar spine—lumbo-sacral junction	0.45
Chest—PA	0.28
Chest—lateral	0.69
Pelvis—AP	0.94

[a] NRPB 1992 *National Protocol for Patient Dose Measurements in Diagnostic Radiology.*
[b] NRPB-SR262 *Normalised Monte Carlo Doses for Medical X-ray Examinations Calculated using Monte Carlo Techniques* (NRPB-SR262).

vertebral morphometry capability may reduce the need for much higher dose radiographic procedures in order to determine degree and extent of vertebral deformities.

The greatest contribution to effective dose from femur and whole body scans is the dose received by the ovaries. However, the genetic risk considered here is not relevant for the majority of the population undergoing bone densitometry assessment since they are generally post-menopausal women. Also, careful positioning by the operator may exclude the ovaries from the primary beam during a femoral neck scan, reducing the effective dose by 16 μSv (29%).

5. Conclusion

We have performed what we believe is the first dose assessment of the Lunar Expert-XL. The results indicate that, where a throughput of four or or more patients per hour is anticipated, a protective screen for the operator may be required.

The effective dose to patients, although exceeding that of pencil beam DXA machines, is much less than standard radiographic procedures, particularly of the lumbar spine. The

pencil beam DXA machines are to be recommended where a standard assessment of bone mineral density is required. However, the Expert-XL has the advantage where reduced scan times, improved image resolution or morphometric analysis of the spine are required and may reduce the need for higher-dose radiographic procedures.

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Original Article

Image Resolution of the Lunar Expert-XL

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Abstract. The Lunar Expert-XL is an example of the latest generation of fan beam densitometers, with the X-ray source and detector array mounted on a C-arm to enable supine lateral imaging. Image resolution for anteroposterior (AP) spine, femur, hand, forearm and lateral morphometry on the Expert-XL were assessed in vitro with the 07-541 Nuclear Associates line pair test pattern. Each scan type was investigated at all available tube currents and scan speeds, and at the maximum, minimum and default bed heights. The effect of soft tissue thickness on resolution was investigated by using varying amounts of Perspex attenuator. The in vitro median lateral (*x*-axis) resolutions at the default bed height for the default scan types were 0.9 line pairs (lps)/mm for the 5 mA fast AP spine and femur scans, and 1.0 lps/mm for 1 mA fast hand, forearm and 5 mA fast morphometry scans. This equates to a resolution of about 1 mm. The best resolution achieved was 1.2 lps/mm (0.83 mm), obtainable on all scan modes with the bed at maximum elevation, but only consistently with the forearm mode. Lower tube current did not affect resolution but did change the range of soft tissue thickness over which an image could be resolved. Turbo scan modes greatly reduced longitudinal (*y*-axis) resolution but had little effect on lateral resolution. This study demonstrates the importance of including an assessment of resolution when validating new equipment, especially if morphometric investigations are to be conducted.

Keywords: Expert-XL; Densitometry; DXA; Quality assurance; Resolution

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Introduction

Effective assessment of bone fracture risk by dual-energy X-ray absorptiometry (DXA) requires accurate and precise information, derived from bone mineral density (BMD) or morphometric examination. The image resolution of DXA limits both image clarity and the ability of edge detection algorithms to distinguish between bone and soft tissue. Digital imaging produces a coarse representation of bone edges, with any edge pixel of an area containing both soft tissue and bone appearing in the image as a composite of both. This produces errors in edge detection, and so leads to inaccuracy in the measured bone area and potentially in calculated BMD [1].

Fan beam densitometers employ an array of detectors for rapid image acquisition. The use of an array eliminates the rectilinear motion required with traditional pencil beam densitometers, so the emitter/detector assembly has only to be moved longitudinally [2]. The increased speed of this system permits the improvement of resolution by the use of smaller detectors in the array and shorter incremental movements of the emitter/detector assembly. Maintaining the same number of counts per detector requires an increase in the overall photon flux and so increases the administered radiation dose, although the effective dose to patients remains well below that of equivalent radiographic procedures [3]. Improved resolution provides more anatomic detail, sufficient to allow morphometric assessment of the spine, although still not sufficient for differential diagnosis.

DXA images are derived by an emitter projecting the object onto the detector. Pencil beam densitometry produces an image of the same relative dimensions as the object. Fan beam densitometry distorts and magnifies the lateral (*x*-axis) dimension of the image by an amount dependent on the distance from the emitter to the object

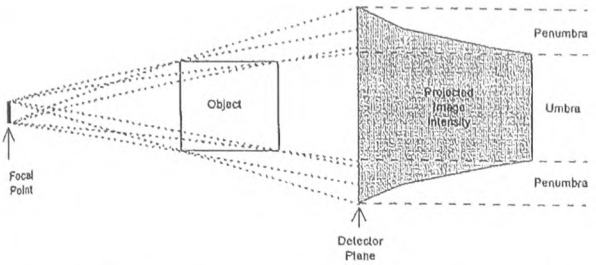


Fig. 1. Diagrammatic representation of the penumbra effect.

and the emitter to the detector. Fan beam distortion produces a lateral penumbra, whose width is determined by the focal point width, the object thickness and the object-to-focal point distance [4] (Fig. 1). However, the longitudinal (*y*-axis) dimensions remain unchanged. Conventional radiographic cone beams distort both the lateral and longitudinal dimensions.

Little work on the resolution of fan beam densitometers has been conducted. Lunar Corporation (Madison, WI) have produced the Expert series of fan beam densitometers, with the initial Expert system released in 1992 being superseded upon the release of the Expert-XL in 1994. Felsenberg et al. [5] have reported a resolution of between 0.95 and 0.7 line pairs (lps)/mm (1.05 and 1.43 mm) for the Expert and 0.7 and 0.5 lps/mm (1.43 and 2.00 mm) for the Hologic QDR 2000+ (Hologic Inc., Waltham, MA). No resolution for the Expert-XL has yet been reported outside the proprietary literature, which states a range of maximal resolutions varying from 2 to 1.6 lps/mm (0.5 mm to 0.625 mm). The aim of this investigation was therefore to measure the image resolution of an Expert-XL in routine clinical use at a district general hospital.

Equipment and Method

Lunar Expert-XL

The Lunar Expert-XL is an example of the latest generation of fan beam densitometers, with both X-ray emitter and detector array mounted on a rotatable C-arm to enable both anteroposterior (AP) and lateral imaging [6]. The emitter assembly consists of a Varian A-I 46 rotating anode X-ray tube, operating at a voltage of 134 keV, with 1 mm of aluminum filtration and a focal spot size of 0.3 mm. The distance from the focal point to the detector array is 112 cm. The detector array contains 288 solid state detectors, each 0.8 mm × 1.6 mm, arranged in two rows. A layer of copper over one row of detectors prevents low energy X-rays from reaching it, thus providing the required discrimination between high and low energies. The Expert-XL can perform eight different investigative procedures at five different sites. It is also possible to vary the X-ray tube current, scan speed and scan width for most procedures. The available investigations are summarized in Table 1. In addition, the scanning table is motorized and the height can be varied between 15.9 cm and 39.2 cm above the detector for optimal image registration and resolution for the type of investigation being performed. The accompanying workstation at this center is equipped with a 21-inch Dell Ultrascan 21TE monitor.

Resolution Test Pattern

Resolution was assessed subjectively using the 07-541 Nuclear Associates (Carle Place, NY) line pair resolution test pattern (Fig. 2a). The 07-541 test pattern contains 15 sets of lead line pairs, arranged horizontally and vertically, covering a range of 0.6 to 3.4 line pairs per milimeter. The test pattern is 0.1 mm thick and is encapsulated in a 3 mm thickness of material mimicking soft tissue.

Method

The five scan types most commonly used in clinical practice were investigated (AP spine, AP femur, forearm, hand, lateral morphometry). The test pattern was imaged at the minimum, maximum and default bed heights for each appropriate scan type. For AP spine and

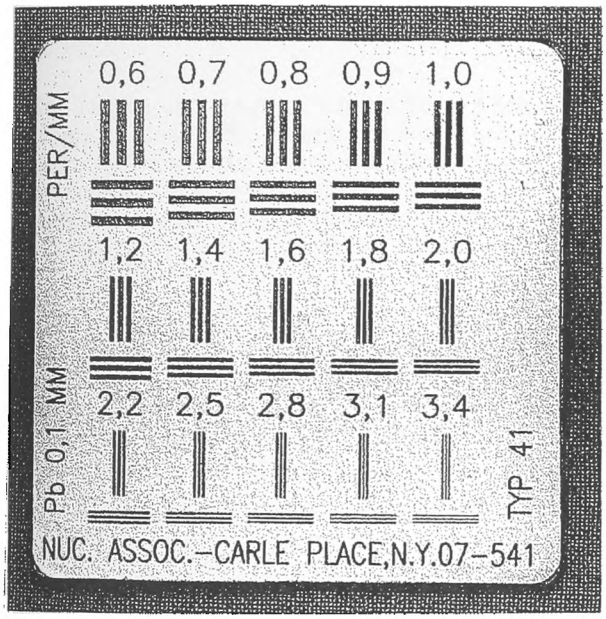
Table 1. Range of settings available for each scan type

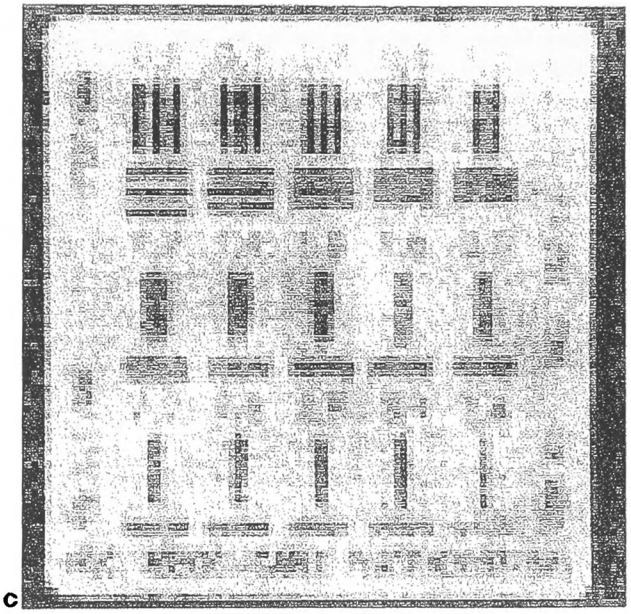
Scan type	Tube current (mA)				Scan speed (s)			Scan width (cm)						
	5	2	1.5	1	Turbo	Fast	Medium	57.6	17.3	14.7	14.4	12.2	11.2	9.4
AP spine	Yes	Yes			7.7	**14.9**			**Yes**	Yes			Yes	
AP femur	Yes	Yes			7.7	**14.9**			Yes	**Yes**			Yes	
Orthopedic hip	Yes	Yes				**16.5**			Yes	**Yes**			Yes	
Lateral spine MM	Yes					**46.5**					**Yes**	Yes		Yes
Lateral spine BMD	Yes					**24.5**					**Yes**	Yes		Yes
Total body			Yes			**119.9**	238.9	**Yes**						
Forearm				Yes		**9.6**					Yes	**Yes**		Yes
Hand				Yes		**18.9**					**Yes**	Yes		Yes

Tube voltage, 134 keV; focal spot size, 0.3 mm; software version, 1.63.
Default scan speeds and widths are shown in **bold** type. Default current settings are dependent on subject mass.
MM: morphometry mode.

AP femur, both 5 mA and 2 mA tube current options were assessed at the default bed heights, but only the 5 mA option was used at the maximum and minimum bed heights. Similarly, when both fast and turbo scan speeds were available, both were used at the default bed height but only the fast speed was used at the maximum and minimum bed heights. For AP spine and AP femur, images were acquired both with and without the mattress on the bed.

The required energy attenuation was achieved by positioning the test pattern between sheets of Perspex (polymethylmethacrylate, also known as Lucite or Plexiglas) which, at the relevant energy levels concerned, have a mass attenuation coefficient of 0.92 relative to lean tissue. Perspex was chosen as it was readily available and simple both to handle and to machine accurately. The initial thickness was determined from that which might be expected clinically for the particular type of scan. The thickness was varied for each scan type in an attempt to determine both the effect on resolution and the range of tissue thickness that could be successfully imaged. For spine and femur scans, the total range of Perspex used was 4–28 cm and 4–20 cm respectively, with 4–8 cm placed beneath the test pattern. For forearm and hand scans, the total range used was 0–12 cm and 0–9 cm respectively, with the Perspex beneath the test pattern varied from 0 to 6 cm for the forearm and 0 to 1 cm for the hand. For hand and forearm acquisitions, the mattress was removed and the forearm positioner placed on the bed, in accordance with normal operating procedure. For the morphometry scan mode, both Perspex and test pattern were stood vertically





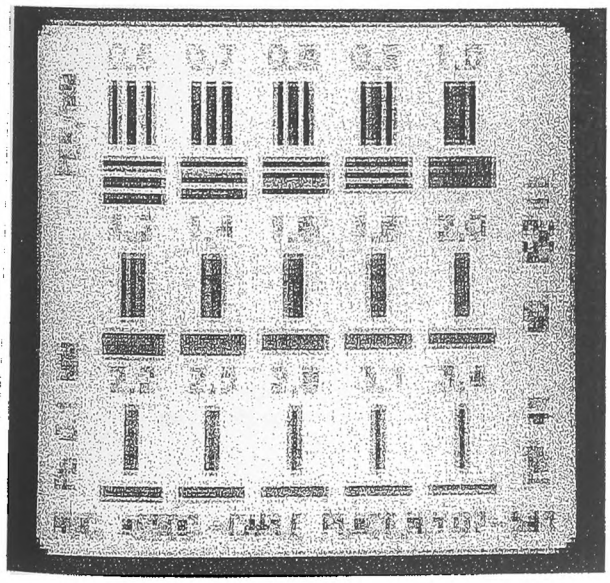


Fig. 2a–c. The Nuclear Associates 07-541 line pair resolution test pattern. **a** Photograph. **b** Resolution on forearm scan mode at maximum bed height, with 3 cm Perspex. **c** Resolution on AP spine mode at default bed height, with 20 cm Perspex.

on a single horizontal Perspex sheet. The total amount of attenuator was varied from 20 to 27 cm, with 10–14 cm on the side closest to the X-ray tube.

Images were analyzed immediately, to allow sufficient time for the X-ray tube to cool before the next acquisition. A single operator manually adjusted the image levels (displayed range), contrast and brightness controls until an optimal resolution was reached. The achieved resolution was measured from the screen, with the image at 300% magnification, and was defined as the last bar section in which a clear distinction could be seen between lines and spaces. The image magnification was sufficient to allow individual image pixels to be easily seen. The expected geometric lateral magnification was also calculated for each scan, taking into account the set bed height and the thickness of underlying Perspex. When the mattress was used for spine and hip acquisitions, an additional 1 cm was added to allow for the thickness of the mattress under compression. For hand and forearm scans, the height of the forearm positioner was added.

Results

The median and range of the resolutions achieved for each scan mode at the default bed height using different depths of Perspex are shown in Table 2. Sample images are shown in Fig. 2b and c. Both 5 mA and 2 mA image acquisitions were found to require a minimum thickness of soft tissue, below which an image could not be formed. As the thickness of soft tissue was then increased, the image became degraded by an increasing scatter component. Although the 2 mA images were visibly poorer than the 5 mA tube current images at large tissue thickness, the measured resolution was found to be approximately equal up to 24 cm of Perspex. Beyond this point the 2 mA images suddenly deteriorated in quality and the resolution was reduced to a level poorer than that which could be measured on the test pattern (i.e., <0.6 lps/mm), whilst the 5mA tube current produced images of 0.7 lps/mm resolution at the maximum soft tissue thickness of 28 cm. The 1 mA hand and forearm modes produced images of 1.0 lps/mm resolution at the maximum tested soft tissue thickness of 12 cm. Resolution was not affected by either the mattress or the forearm positioner.

Tube current had little effect on the achievable resolution, provided the current chosen was appropriate for the amount of soft tissue present in the region of interest. Accordingly, the tube current did change the range of tissue thickness over which an image could be resolved: from 9 to at least 28 cm Perspex for 5 mA, from 5 to 24 cm for 2 mA, and from 0 to at least 12 cm for 1 mA. The use of the turbo scan speed dramatically degraded the longitudinal resolution but did not cause any significant decrease in lateral resolution.

Scan speed did not appear to have much effect on lateral resolution. The median and range of lateral resolution for the AP femur scan were the same for both fast and turbo scan speeds at both 5 mA and 2 mA (median 0.9 lps/mm, range 1.0–0.8 lps/mm). For the AP

Table 2. Image resolution of the Expert-XL at default bed height settings

Scan mode		*n*	Resolution (lps/mm)[a]				Perspex attenuator (cm)[b]	
Tube current (mA)	Speed		Lateral		Longitudinal		Range tested	Minimum required for image
			Median[c]	Range	Median[c]	Range		
AP spine								
5	Fast	24	0.9	0.7–1.0	0.8	<0.6–0.9	5–28	9
	Turbo	11	0.9	<0.6–0.9	<0.6	<0.6	5–28	9
2	Fast	13	0.8	0.6–0.9	0.8	<0.6–0.9	4–28	5
	Turbo	10	0.9	<0.6–1.0	<0.6	<0.6	4–28	5
AP femur								
5	Fast	10	0.9	0.8–1.0	0.9	0.7–0.9	5–20	9
	Turbo	10	0.9	0.8–1.0	<0.6	<0.6	5–20	9
2	Fast	10	0.9	0.8–1.0	0.8	0.7–0.9	4–20	5
	Turbo	10	0.9	0.8–1.0	<0.6	<0.6	4–20	5
Hand								
1	Fast	10	1.0	1.0–1.2	1.0	1.0–1.0	0–9	0
Forearm								
1	Fast	10	1.0	1.0–1.2	1.0	0.9–1.0	0–12	0
Morphometry								
5	Fast	12	1.0	1.0–1.2	0.7	<0.6–0.7	20–27	<20

[a]There are 15 discrete line pairs on the 07-541 test pattern, ranging from 0.6 to 3.4 line pairs per millimetre (lps/mm). Resolution in lps/mm = 1/(resolution in mm). In the table, 0.6, 0.7, 0.8, 0.9, 1 and 1.2 lps/mm correspond to 1.67, 1.43, 1.25, 1.11, 1.00 and 0.83 mm.
[b]Ratio of attenuation coefficients between Perspex and lean tissue = 0.92.
[c]Acquisitions that did not produce viable images were excluded from median calculations.

Table 3. Image resolution of default scan types at minimum, default and maximum bed elevation

Scan mode	*n*	Bed height (cm)[a]	Object distance from detector array (cm)[b]	Expected lateral magnification[c]	Resolution (lps/mm) Lateral		Longitudinal	
					Median	Range	Median	Range
AP spine	10	0.2 (minimum)	20.7–24.7	1.23–1.28	0.9	0.7–0.9	0.8	<0.6–0.9
(5 mA fast)	24	–2.0 (default)	22.9–26.9	1.26–1.32	0.9	0.7–1.0	0.8	<0.6–0.9
	10	–23.5 (maximum)	44.4–48.4	1.66–1.76	1.1	0.8–1.2	0.9	0.8–1.0
AP Femur	10	0.2 (minimum)	20.7–24.7	1.23–1.28	0.8	0.7–0.9	0.9	0.7–0.9
(5 mA fast)	10	–2.0 (default)	22.9–26.9	1.26–1.32	0.9	0.8–1.0	0.9	0.7–0.9
	10	–23.5 (maximum)	44.4–48.4	1.66–1.76	1.0	1.0–1.2	0.9	0.8–1.0
Hand	10	0.2 (minimum)	19.5–20.5	1.21–1.22	0.9	0.8–0.9	0.9	0.9–1.0
(1 mA fast)	10	–17.5 (default)	37.2–38.2	1.50–1.52	1.0	1.0–1.2	1.0	1.0–1.0
	12	–23.5 (maximum)	43.2–44.2	1.63–1.65	1.0	1.0–1.2	1.0	0.9–1.2
Forearm	10	0.2 (minimum)	19.5–25.5	1.21–1.29	0.9	0.8–0.9	1.0	0.9–1.0
(1 mA fast)	10	–17.5 (default)	37.2–43.2	1.50–1.63	1.0	1.0–1.2	1.0	0.9–1.0
	10	–23.5 (maximum)	43.2–49.2	1.63–1.78	1.2	1.0–1.2	1.0	0.9–1.0
Morphometry								
(5 mA fast)	12	–15.5 (default)	40	1.56	1.0	1.0–1.2	0.7	<0.6–0.7

[a]As defined by Lunar Software, where height = 0 is the minimum height permitted by the hardware. Software limits the height to 0.2 cm above this.
[b]Includes thickness of underlying Perspex. Hand and forearm scan modes include elevation caused by the forearm positioner. AP spine and femur calculations assume a compressed mattress thickness of 1 cm.
[c]Calculated from: focal point-to-detector distance/focal point-to-object distance. Distance from the tube focal point to the detector array = 112 cm.

spine scan, the median lateral resolution of the 2 mA fast scan was slightly inferior to the turbo mode (0.8 lps/mm for 2 mA fast, 0.9 lps/mm for 2 mA turbo). However, scan speed produced a clear effect on longitudinal resolution, with no turbo scan achieving a resolution that could be measured on the test object (resolution <0.6 lps/mm).

Bed elevation produced a direct effect on the lateral resolution, as shown in Table 3. Included in the table is a calculation of the geometric fan beam lateral magnification for each bed height. The estimate takes into account the thickness of Perspex underlying the test pattern, and the height of the forearm positioner is included for the hand and forearm modes. A maximum lateral resolution of 1.2 lps/mm was achieved on the forearm, hand and morphometry scan modes with the bed at the default height, and on all modes with the bed at the maximum elevation. The median lateral resolutions varied at the maximum bed elevation, with 1.1 lps/mm for AP spine, 1.0 lp/mm for AP femur and hand, and 1.2 lps/mm for the forearm. As expected, the poorest lateral resolutions, of 0.9–0.7 lps/mm, occurred at minimum bed elevation.

Surprisingly, longitudinal resolution was also improved slightly by bed elevation. The median resolutions for the AP spine scan improved from 0.8 lps/mm (range: 0.9 to <0.6 lps/mm) at the minimum bed height to 0.9 (1.0 to 0.8) lps/mm at the maximum. The median resolutions for the AP femur scan were the same (0.9 lps/mm) at both minimum and maximum bed heights, but the range varied from 0.9–0.7 lps/mm at the minimum bed height to 1.0–0.8 lps/mm at the maximum. The hand mode also showed improvement, from a median and range of 0.9 (1.0–0.9) lps/mm at the minimum bed height to 1.0 (1.2–0.9) lps/mm at the maximum. The forearm mode was an exception to the trend, with no change in median or range of resolution over the full variation in bed height.

Discussion

This investigation has demonstrated the image resolution achievable on the Expert-XL over the range of investigations that may typically be performed as part of a clinical investigation. Lateral resolution was found to be strongly influenced by bed height, whilst longitudinal resolution was slightly influenced. For comparison, we attempted to determine the resolution of the Lunar DPXL pencil beam using the same phantom, but failed. Even on the highest resolution mode the DPXL was not able to image the coarsest line pair pattern of 0.6 lps/mm, thus indicating a resolution of poorer than 1.67 mm. The 07-541 test pattern provides only a discrete and subjective measure of resolution within a limited range. Assessment of pencil beam resolution would require a coarser line pair test pattern.

It was expected that as soft tissue thickness increased, the resolution of lower tube current scans would deteriorate faster than those performed with a higher tube current. Although increasing thickness of soft tissue visibly produced more random scatter in the image, the 07-541 line pair test pattern did not reveal the effect of scatter on the resolution. As a result, it was not possible to identify the optimum ranges of soft tissue thickness for each tube current, only the absolute range. A hole phantom might better demonstrate the effect of scatter

but would be less susceptible to the penumbra effect, making it inappropriate for measuring the effect of bed height upon resolution.

At a tube current of 5 mA, the Expert-XL produced a viable image in vitro at a Perspex thickness ranging from 9 cm to at least 28 cm. However, under normal use BMD values are calibrated to be accurate within an expected thickness of soft tissue, based on the subject's weight and the anatomic region of interest. If the actual thickness of soft tissue differs greatly from the expected, the calculated BMD value will be inaccurate. Although Perspex provides a close attenuation match to lean tissue at the X-ray energies used, the difference is sufficient to require caution when extrapolating between in vitro and in vivo applications.

Lateral resolution showed improvement with increasing bed elevation, although not to the extent that might be expected for the degree of geometric magnification. It seems likely that the degradation of the image was due to the thickness of soft tissue used, but this could not be demonstrated convincingly with the 07-541 test pattern. In general, although lateral resolution can be improved by the elevation of the object, there is a limit. As an object is moved toward the source of a fan beam, the beam is concentrated on a smaller target area, increasing the localized dose. Additionally, if the object is of finite depth, layers of the object at different depths are magnified by different amounts, so producing a penumbra (area of partial shadow) around the object. The width of the penumbra depends on the thickness of the object and the width of the focal spot, as well as the distance from the object to both the source and the detector. Penumbra, projection and radiation dose increase as an object approaches the source. Optimal lateral resolution is therefore a balance between the positive influence of the projection effect against the negative factors of the penumbra effect and radiation dose. The manufacturer's default bed heights for each scan mode place the region of interest at an imaging plane determined, presumably, from consideration of these factors.

Unexpectedly, the longitudinal resolution also showed some improvement with bed elevation, most noticeably with the range of resolutions achieved with the AP spine and femur investigations. This was most probably due to scatter, as the AP spine and femur investigations included the greatest thickness of soft tissue. Resolution is degraded when a photon interacting with an object is deflected rather than absorbed, and still reaches the detector. If the angle of deflection is too great, the photon misses the detector altogether, so is not present in the final image. As the distance from the detector to the object decreases, the range of angles of scattered photons reaching the detector is increased, reducing resolution. The longitudinal resolution is therefore dependent on detector element length and scan speed, as well as the object's distance from the detector and relative attenuation characteristics.

Clinically, resolution is important for both BMD and morphometric studies. BMD studies employ an edge detection algorithm to differentiate between bone and soft tissue, but the efficacy of the algorithm is limited by the resolution. Poor resolution produces a coarse representation of bone edges, leading to a potential misidentification by the automated point-typing algorithm. Higher-resolution densitometry systems should therefore provide better estimates of bone area. This has been demonstrated by Bärenholdt et al. [7], who found a better bone area estimate for the Expert than for the QDR 4500, although other factors may still be involved. Vertebral morphometry studies depend on good resolution to adequately identify the edges of the vertebral bodies. A large-scale MXA reference data study by Rea et al. [8] compared MXA with radiography and found some difference with corresponding wedge and biconcave ratios, but not with crush ratios. In addition, they also reported small but statistically significant differences between the DXA systems used (three Hologic QDR 2000+ and one QDR 4500). Two phantom-based studies at this center have demonstrated that the Expert-XL underestimates the severity of biconcavities by an average of 8% [9], and furthermore that small angles of spinal malalignment (2.5°) can produce an increase in the measured vertebral height [10]. The system resolution was identified as a potential cause of both errors. Resolution varies between modalities (MXA and radiography) and between DXA systems; therefore machine-specific MXA reference data may be required.

The resolutions across the width of the fan beam that might be expected using the Expert-XL at the respective default bed heights are 0.9 lps/mm for the AP spine and femur, and 1.0 lp/mm for the hand, forearm and vertebral morphometry investigations. For the fast scan speed, the longitudinal resolutions at the respective default bed heights are 0.8 lps/mm for the AP spine, 0.9 lps/mm (at 5 mA) or 0.8 lps/mm (at 2 mA) for the AP femur, 1.0 lp/mm for the hand and forearm, and 0.7 lps/mm for vertebral morphometry. Using the turbo scan speed, the longitudinal resolution is always poorer than 0.6 lps/mm, irrespective of the site of interest. The maximum lateral and longitudinal resolution achieved by this investigation is 1.2 lps/mm, equivalent to 0.83 mm, but only the lateral resolution of forearm scans with the bed at maximum elevation consistently achieves this level. The resolution attained with the machine at this district general hospital does not concur with the 2–1.6 lps/mm (0.5–0.625 mm) reported by the manufacturer, but the resolution achieved is superior to that of the DPXL pencil beam densitometer. However, even at the highest bed elevation, the measured resolution of the Expert-XL does not approach the approximately 3.5 lps/mm (0.29 mm) resolution reported for lateral spine radiography by Felsenberg et al. [5]. When considering use of improved DXA technology for morphometric purposes, determination of the resolution should be considered as part of the validation procedure.

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A phantom for evaluating bone mineral density of the hand by dual-energy x-ray absorptiometry

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Abstract. Dual-energy x-ray absorptiometry (DXA) is a precise, widely used method for measuring bone mineral density (BMD), usually of the lumbar spine and femoral neck. Recent developments, such as a lower x-ray tube current and pixel by pixel analysis, enable smaller bones and thinner tissue volumes, as in the hand, to be measured. Measurements of hand bone mineral content (BMC) and BMD could be useful in assessing disease severity in early rheumatoid arthritis and in monitoring disease progression and response to therapeutic intervention. A phantom is required for evaluating the software, measuring long-term precision and comparing with other DXA methods.

This note describes the design and evaluation of a hand phantom for use on a Lunar DPX-L dual-energy x-ray absorptiometer. The phantom consists of three sections representing the metacarpals, and proximal and distal phalanges, using aluminium and Perspex as the bone and lean tissue equivalents respectively. The BMD of the three sections is approximately 1.0, 0.6 and 0.3 g cm^{-2}. The phantom demonstrates limitations in the potential accuracy of BMD determination at low densities using the Small Animal Software on the Lunar DPX-L. Improved recognition of low-density regions was obtained with the Lunar EXPERT with precision values of 0.9, 1.1 and 2.0% for the three sections of the phantom respectively.

Keywords: hand, phantom, bone densitometry, DXA

1. Introduction

Dual-energy x-ray absorptiometry (DXA) is a precise, widely used method for measuring bone mineral density (BMD, g cm^{-2}) to assess osteopenia and osteoporosis, usually of the lumbar spine and femoral neck. DXA is based on the attentuation of two x-ray energies by the body. The degree of attenuation depends on the beam characteristics in addition to the thickness and density of the material through which the rays pass. The theory of DXA assumes that there are only two substances in the region being measured, i.e. bone and soft tissue, requiring therefore two different energies to allow discrimination. The soft tissue is assumed to be of constant composition within the region being measured. The x-ray energies are chosen to optimize the differential attentuation between bone and soft tissue while minimizing the radiation dose to the patient. The optimal energies are 40–45 keV for the lower-energy photons and 75 keV for the higher (Rutt 1985). The DXA system in our centre, the Lunar DPX-L, uses a tube current of 750 or 3000 μA for performing scans of the lumbar spine and femoral neck. The analysis software identifies the regions of interest, for

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which BMD values will be calculated, and the soft-tissue baseline, to enable the attenuation due to soft tissue to be subtracted from the calculation. A minimum of 12 cm soft tissue throughout the scan region is required to calculate correct tissue baselines (Lunar). Recent developments in DXA such as a lower tube current of 150 μA and pixel by pixel analysis enable smaller bones and thinner tissue volumes to be measured.

The software available for the Lunar DPX-L machines utilizing these developments is called Small Animal Software and is intended for research use in assessing BMD, BMC (bone mineral content) and area of total body or appendicular bones in small animals. This software is designed for animals of 0.15–5 kg but with a minimum of 3.8 cm tissue depth within the region being measured for total-body composition (Lunar). This suggests that soft-tissue equivalent material may need to be added when using this technique for the human hand. Measurement of hand BMC and BMD could be useful in assessing disease severity in early rheumatoid arthritis, in monitoring disease progression and response to therapeutic intervention (Deodhar *et al* 1994, Peel *et al* 1994, Florescu *et al* 1993). A phantom is required for evaluation of this software for use in the measurement of BMC and BMD in the human hand, for measuring long-term precision and for comparison with other DXA methods.

An aluminium spine phantom is supplied with the Lunar DPX-L. This is a 16 cm $\times$ 4 cm block of aluminium of varying thickness representing the first four lumbar vertebrae. The lowest BMD of this phantom is approximately 0.9 g cm^{-2} and the phantom has raised edges to facilitate edge detection. This, therefore, cannot assess the precision of the system in the range of BMD encountered in the human hand and does not provide the same challenge to the edge detection algorithm as the small, almost rounded phalanges. The European Spine Phantom (ESP), although being anthropomorphic in shape with respect to the spine, is not designed to approximate the situation in the hand. Consequently, the lowest BMD (0.5 g cm^{-2}) is also too high and the soft-tissue equivalent block in which the vertebral components are imbedded provides soft-tissue attenuation which approximates that of 20 cm of human tissue, far more than is present in the human hand. The European Forearm Phantom (EFP) is similarly designed to approximate the forearm. Again, the BMD of 0.5–1.5 g cm^{-2} does not encompass the lower values found in the hand. This paper describes the specification and design of a hand phantom for use with the Lunar DPX-L Small Animal Software and includes results of measurement on the Lunar DPX-L and the newer Lunar EXPERT fan beam densitometer.

2. Methods and results

2.1. The Hull hand phantom

2.1.1. Phantom requirements. The aim was to design a phantom to assess precision and linearity of the system at low BMD values (0.3–0.9 g cm^{-2}). A simple geometric shape was desired rather than an anthropomorphic one as the phantom is also required to monitor long-term precision. A more complex shape would introduce more operator variability at the analysis stage. It was decided with this pilot design to use a mean of 3.8 cm of soft-tissue equivalence as recommended. This also enabled us to correlate the results with those of the forearm software on the same machine.

2.1.2. Choice of materials. The phantom was constructed from two materials simulating homogeneous soft tissue and bone mineral respectively. The choice of material was based upon the attenuation co-efficients, availability, construction considerations and cost.

Aluminium was chosen as the bone mineral substitute. The ratio of the mass attenuation co-efficient (μ/ρ) for aluminium to bone mineral is about 0.9 at x-ray energies of 10 keV–1 MeV. Perspex was chosen as the soft tissue and bone marrow substitute. The ratio of mass attenuation co-efficient for Perspex to lean tissue rises from 0.8 at 35 keV to 1.04 at 1 MeV (HPA 1977). Perfect tissue substitutes would have ratios of 1.0.

2.1.3. Design and construction. The design consists of aluminium tubes with a Perspex core simulating bone marrow within the medullary cavity. Hollow cylindrical tubes were chosen so as to mimic the cross sectional attenuation profile of the metacarpals and phalanges. The ability of the software to correctly detect the edges of a structure, closely resembling that encountered in the bones of the hand, can thus be tested. The relative diameters of aluminium tubes to Perspex rod were determined experimentally to give BMDs of about 0.8, 0.5 and 0.2 g cm^{-2}. The external dimensions of the 3 sets of tubes are 20 mm × 100 mm, 15 mm × 50 mm and 12 mm × 50 mm. These are embedded in a Perspex block to ensure mean equivalent soft tissue thickness of 3.8 cm as recommended when using the Small Animal total-body mode (Lunar). The phantom consists of three sections, representing the metacarpals, proximal phalanges, and middle and distal phalanges. Each section was also designed to be of different BMD representing the healthy normal and early and late stages of rheumatoid arthritis.

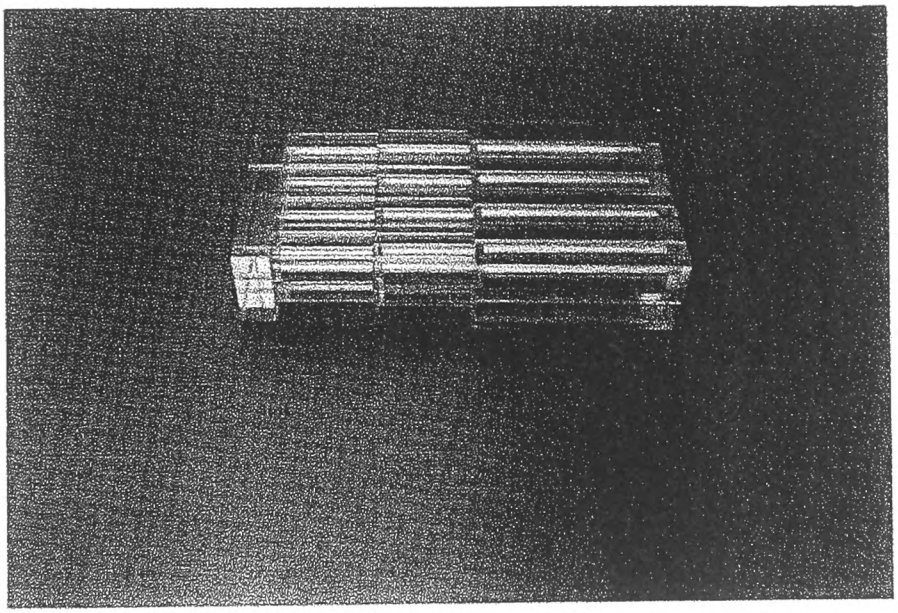

Figure 1. A photo of the hand phantom positioned on the DPX-L couch.

The phantom was constructed from a single block of Perspex drilled for insertion of the aluminium tubes (figure 1). Perspex spacers are positioned between the three sets of tubes, simulating the joint spaces. The dimensions of the aluminium tubes, and the inter-tube dimensions are, of course, known and this enables checking of the accuracy of, for example, measurements of joint spaces.

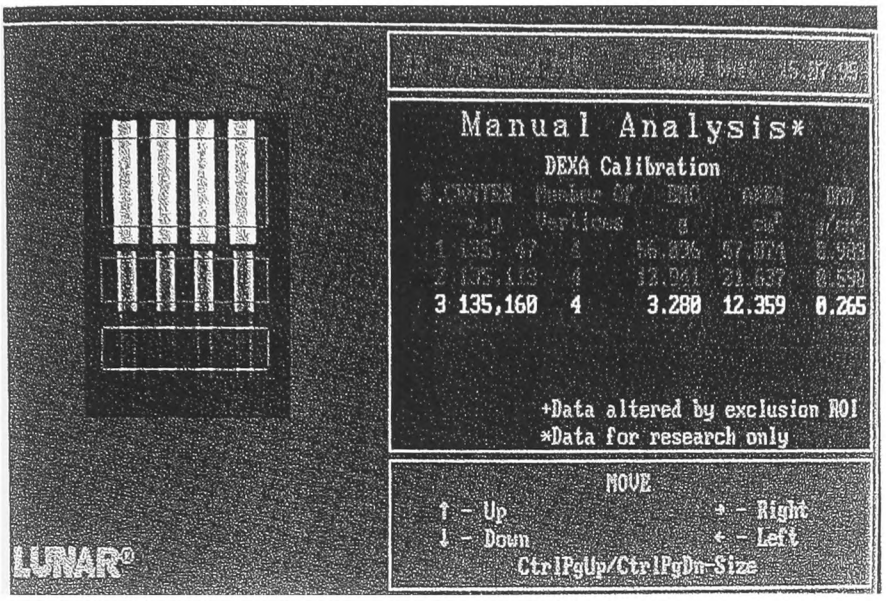

Figure 2. A DPX-L image achieved using Small Animal Software in high-resolution, slow mode with the three regions of interest identified.

2.2. Hand phantom measurement on a Lunar DPX-L

The phantom was placed directly on the scan table, aligned with the central axis and scanned using the Lunar Small Animal total-body software on a Lunar DPX-L. Ten scans of the phantom were performed over a period of 2 weeks using detail medium- and detail slow-scan modes. The scan and processing time involved using the other scan modes (high-resolution medium and high-resolution slow, of 45 min and 1 h respectively) was considered prohibitive in terms of the additional information this would provide. Only five scans were performed for the latter two modes, each over a period of 1 week. Analysis was performed using rectangular regions of interest placed over the three sections of the phantom. The regions of interest were of the same dimensions and locations on all scans (figure 2). The mean (standard deviation) BMD of the high-density region rises from 0.947 (0.021) g cm^{-2} using detail medium-scan mode to 0.990 (0.003) g cm^{-2} using the high-resolution slow-scan mode. There is a similar rise in the BMD of the medium-density area from 0.564 (0.019) to 0.609 (0.004) g cm^{-2}. The BMD for the low-density area falls from 0.310 (0.008) to 0.266 (0.003) g cm^{-2} using the detail medium and high-resolution slow mode respectively. The mean BMDs and precision, as percentage coefficients of variation, are shown in table 1. The mean values for the BMC of all three regions increased slightly from detail medium to high-resolution slow mode (table 2). The area within each region of interest defined by the software as containing a bone equivalent material is shown in table 3. The actual projected areas were 62.4 cm^2 for region one, 22.76 cm^2 for region two and 17.29 cm^2 for region three.

BMD measurement of the forearm using DXA is an accepted, widely used procedure. For comparison, the hand phantom was also scanned using the forearm software (fast speed) on the same machine. The forearm acquisition mode uses the same tube current of 150 μA and pixel size of 0.6 by 1.2 as the Small Animal high-resolution slow mode. The phantom

Table 1. Mean (standard deviation) and precision (% CV) of BMD for the three regions of interest assessed using the four scan modes of the Lunar Small Animal Software.

		Metacarpals		Proximal phalanges		Distal phalanges	
Scan mode	*n*	BMD (g cm^{-2}) mean (s.d.)	% CV	BMD (g cm^{-2}) mean (s.d.)	% CV	BMD (g cm^{-2}) mean (s.d.)	% CV
det. med	10	0.947 (0.021)	2.21	0.564 (0.019)	3.34	0.310 (0.008)	2.62
det. slow	10	0.949 (0.017)	1.88	0.575 (0.023)	4.07	0.306 (0.006)	1.83
hires. med	5	0.984 (0.002)	0.17	0.606 (0.002)	0.39	0.279 (0.002)	0.74
hires. slow	5	0.990 (0.003)	0.33	0.609 (0.004)	0.71	0.266 (0.003)	1.04

Table 2. Mean (standard deviation) and precision (% CV) of BMC for the three regions of interest assessed using the four scan modes of the Lunar Small Animal Software.

		Metacarpals		Proximal phalanges		Distal phalanges	
Scan mode	*n*	BMC (g) mean (s.d.)	% CV	BMC (g) mean (s.d.)	% CV	BMC (g) mean (s.d.)	% CV
det. med	10	57.88 (1.55)	2.68	12.74 (0.44)	3.46	2.02 (0.40)	19.81
det. slow	10	58.07 (1.60)	2.76	12.91 (0.49)	3.84	1.98 (0.48)	24.01
hires. med	5	60.80 (0.14)	0.24	13.77 (0.05)	0.39	3.58 (0.04)	1.10
hires. slow	5	61.23 (0.23)	0.38	13.81 (0.10)	0.72	3.68 (0.15)	4.20

Table 3. Mean (standard deviation) and precision (% CV) of measured area for the three regions of interest assessed using the four scan modes of the Lunar Small Animal Software. Actual projected areas containing 'bone' within each region are indicated.

		Metacarpals		Proximal phalanges		Distal phalanges	
Scan mode	*n*	Area (cm^2) mean (s.d.)	% CV	Area (cm^2) mean (s.d.)	% CV	Area (cm^2) mean (s.d.)	% CV
det. med	10	60.81 (0.85)	1.39	22.57 (0.37)	1.62	6.48 (1.15)	17.82
det. slow	10	61.21 (0.78)	1.28	22.45 (0.39)	1.75	6.47 (1.49)	23.01
hires. med	5	61.81 (0.06)	0.10	22.74 (0.01)	0.03	12.85 (0.11)	0.88
hires. slow	5	61.84 (0.06)	0.10	22.70 (0.03)	0.14	13.64 (0.42)	3.10
Actual projected area		62.40		22.76		17.29	

was scanned with and without the Delrin forearm positioning plate. By fixing the scan width to encompass only two of the aluminium rods, mimicking the radius and ulna, the phantom was suitable for use with the forearm analysis software. Rectangular regions of interest were positioned over the highest-BMD section (metacarpal), yielding BMD values of 0.767 and 0.755 g cm^{-2} with and without the positioning plate respectively. These are significantly lower than the BMD value of 0.992 g cm^{-2} obtained for the same region using the highest-resolution scan mode within the Small Animal Software.

2.3. Hand phantom measurement on a Lunar EXPERT

The Lunar EXPERT calculates BMD values using dual-energy x-rays as for the Lunar DPX-L machine but, using a higher tube current and smaller sampling size, producing high-resolution images of almost radiographic quality. This system has acquisition and analysis capabilities specifically for the hand. The hand phantom was placed on the forearm positioner and scanned using the 1 μA fast mode with the table set at the manufacturer's recommended height. Analysis was performed using three rectangular regions of interest as for the DPX-L (figure 3). The analysis software on the EXPERT machine incorporates a facility to display the characterization of individual pixels, i.e. whether the software has coded them as bone, soft tissue, air, neutral or artefacts. Any pixel incorrectly characterized can be manually redefined.

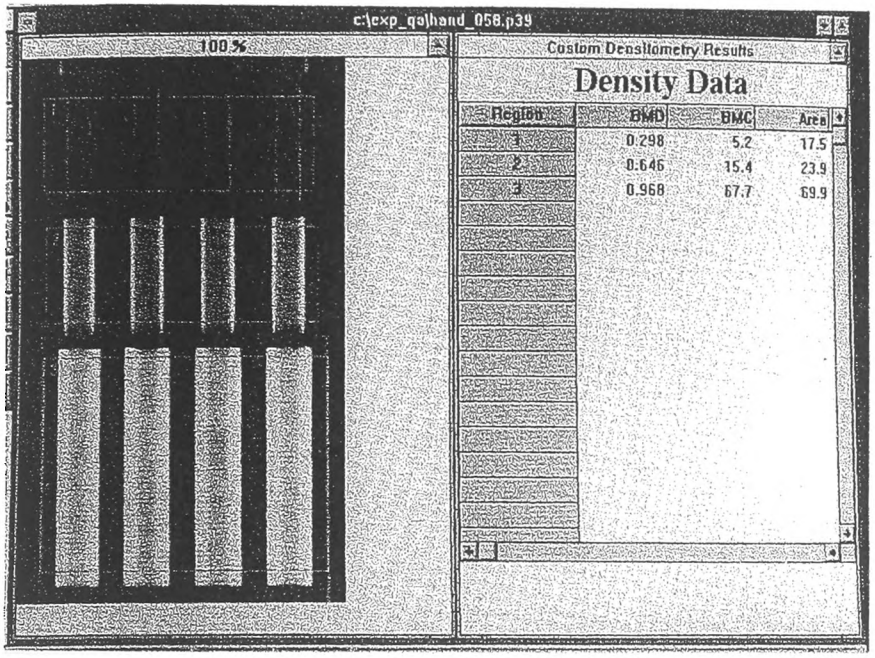

Figure 3. An EXPERT image achieved using hand acquisition mode with the three regions of interest identified.

The Lunar EXPERT correctly categorized all pixels as being bone or soft tissue and no adjustments were required. The hand phantom was scanned daily over 23 weeks on the EXPERT machine: the mean BMD (precision, CV %) values are 0.972 g cm^{-2} (0.9%) for the metacarpal region, 0.646 g cm^{-2} (1.1%) for the proximal phalanges region and 0.292 g cm^{-2} (2.0%) for the distal phalanges region.

3. Discussion

Using Lunar Small Animal Software on the DPX-L, the BMD for the metacarpal and proximal phalanges regions increases slightly with increasing resolution of the measurement but that for the distal phalanges region decreases. The mean precision (% CV) for each scan mode was 2.7% for detail medium, 2.6% for detail slow, 0.43% for high-resolution medium

and 0.69% for high-resolution slow. The difference in BMD between the different scan modes may be due to a difference in measured BMC and/or area. The bone mineral content of the three regions follows a similar pattern with a slight increase with increasing resolution. This may be due to the partial-volume effect of the larger pixels of lower-resolution scans containing part bone and part soft tissue at the boundaries.

The areas determined by the software to contain bone or bone equivalent material within the metacarpal region of interest and the proximal phalanges region of interest were approximately equal to the actual areas of aluminium within each of those regions using all four scan modes. The software thus appears to correctly identify the boundaries of the aluminium tubes in these two regions of the phantom having BMD of approximately 0.95 and 0.6 g cm^{-2}. However, the areas determined for the distal phalanges region, of actual area 17.3 and BMD of 0.3 g cm^{-2}, were at best an underestimate of 21% (13.6 cm^2) and at worst 62% (6.5 cm^2). The system, therefore, is not defining the whole of the aluminium tubes within this area as 'bone' and, as BMD is BMC/area, the measured BMD may also be inaccurate. As the software does not enable display or adjustment of pixel categorization, it is difficult to determine whether the error is occurring at the outer edges or in the Perspex filled centre of the tubes and there is no mechanism to correct for it. The density of these smaller tubes appears to be below a software defined bone threshold on the DPX-L machine.

The Small Animal high-resolution slow mode and forearm software (fast) use the same tube current of 150 μA and pixel size of 0.6 mm × 1.2 mm and the software determined areas in each case are similar to the actual area. However, there is a significant difference in the estimate of BMD between the forearm and Small Animal Software.

Using the point typing facility on the Lunar EXPERT it was possible to confirm that all the aluminium components of the hand phantom were correctly identified as being bone pixels even at densities as low as 0.3 g cm^{-2}. The long-term precision as percentage coefficient of variation for the high-, medium- and low-BMD regions over a period of 23 weeks was 0.9, 1.1 and 2.0% respectively. The BMD estimated by the Lunar EXPERT is similar to that of the DPX-L for both the metacarpals and distal phalanges. However, the BMD of the proximal phalanges region appears significantly higher on the EXPERT. Due to inaccuracies noted in area determination on the DPX-L, this discrepancy is more likely to be due to an underestimate of BMD on that machine.

4. Conclusion

The hand phantom described covers the range of BMD likely to be experienced in clinical practice and enables monitoring of precision and linearity at these low densities. It was designed for use on the Lunar DPX-L but should be suitable for dual-energy x-ray machines using similar x-ray energies. Studies are now under way involving the measurement of this phantom on a range of machines. It is not designed as a truly anthropomorphic phantom and cannot be used to assess accuracy of BMD measurement as it has not been calibrated against standards of known bone density.

The phantom demonstrates some limitations in the potential accuracy of BMD determination at low densities using the Lunar DPX-L. A facility to display profiles, as is available with DPX-L AP spine software, or point typing as on the EXPERT, could enable these errors to be detected and corrected. The phantom also demonstrates differences in BMD when estimated using different software packages on the Lunar DPX-L.

The Lunar EXPERT correctly identifies all aluminium components as being bone pixels even at densities as low as 0.3 g cm^{-2} with a precision of 0.9–2% at the range of BMD values used in the phantom.

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Osteoporosis International

'iginal Article

velopment and Evaluation of a Phantom for Morphometric X-ray ısorptiometry

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tract. Morphometric X-ray absorptiometry (MXA) 'ides the potential to assess vertebral deformity using :chnique with much lower radiation dose to the ent than standard radiographic procedures. MXA 'comes many other limitations such as cone beam ɔrtion observed in conventional plane radiographs. A ıtom has been designed to assess the accuracy of the A technique, to monitor long-term precision and to ss inter- and intra-operator variability. The phantom sists of two columns of 12 cylinders representing the ebral bodies, one of regular components and one esenting vertebral deformities. Each column may be rted, as required, into a Perspex torso-mimicking k. Initial assessment on the Lunar Expert-XL ıonstrates that the phantom provides image para- ers reflecting those found clinically. Measurement of ebral height was found to be consistently under- mated by 4.9%. Operator precision ranged from 0.6% posterior height measurement to 1.0% for middle ght measurement of the regular component column. corresponding precision range for the column esenting vertebral deformation was 0.6% (posterior) 1.1% (middle). Analysis of 10 scans of each column two independent operators demonstrated a few ificant differences in height assessment confined to 'thoracic' region of the regular column. However, r-operator variability was found to increase with easing complexity of vertebral shape producing eral differences, particularly in posterior height essment of the deformed column.

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Keywords: Morphometric X-ray absorptiometry; Osteoporosis; Phantom; Quality assurance; Spine; Vertebral morphometry

Introduction

Osteoporosis-related fractures usually occur in the wrist, hip or spine. Those of the wrist and hip are usually readily confirmed using standard X-ray procedures, but those of the spine rarely present for clinical diagnosis. Vertebral deformity fractures are identified as a change in vertebral shape and may be classified as wedge, biconcave or crush and as grade 1, 2 or 3 [1,2] (Fig. 1). The grading may be based on percentage reduction in anterior, middle and/or posterior height [1], deviation from a defined normal range [2] or as a ratio of height to predicted height based on that of adjacent vertebrae [3]. Generally a 25% reduction in height or 3 SD from normal or predicted values is used as the cut-off point for defining a fracture.

The standard method of assessing vertebral deformity using lateral radiographs of the lumbar and thoracic spine is associated with a radiation dose to the patient of about 800 μSv [4]. Two exposures are necessary due to differences in attenuation in the lumbar and thoracic regions. The images produced are prone to magnification and distortion due to the cone beam geometry. The consequent elliptical appearance of the upper and lower borders of each vertebra and the relative distortion of vertebral height can make measurement problematic and therefore assessment of vertebral compression difficult. Patients are placed in the decubitus position for this technique making positioning difficult and repeat films

Fig. 1. Classification of vertebral deformities.

frequent, which adds to the radiation dose. Interpretation of lateral spine radiographs is generally a visual semi-quantitative assessment by a radiologist. More quantitative assessment may be performed by digitizing the radiograph and obtaining the anterior, posterior and mid-vertebral height, and several studies have investigated the correlation with readings performed by radiologists [5,6].

The recent development of morphometric X-ray absorptiometry (MXA) potentially overcomes some of the limitations of conventional plane radiographs. One of the machines providing this capability is the Lunar Expert-XL (Lunar, Madison, WI). This uses a fan beam of X-rays and a solid state detector. The X-ray tube and detector assembly are mounted on a C-arm which may be rotated to enable lateral imaging of the spine with the patient in a supine position, hence reducing distortion due to vertebral sagging in the lumbar region sometimes seen on conventional X-ray images. The C-arm scans axially from the level of L5 up to T4 producing a single image of the spine, making identification of vertebral levels easier. The superior to inferior distortion with this method should be negligible and any anteroposterior (AP) magnification should not interfere with assessment of vertebral height. We have assessed the effective dose from this technique to be 71 μSv [7], about 9% of that for conventional lateral spine radiographs. However, due to the lower resolution of the Expert-XL of approximately 1 line pair per millimeter (measured on our system), compared with the 3.5 line pairs per millimeter of conventional radiography [8], X-ray images are considered mandatory where other pathology is suspected.

A phantom is required to assess the accuracy of the MXA technique, to monitor long-term precision and to assess inter- and intra-operator variability. Currently there is no suitable phantom available. The aluminum spine phantom supplied with the machine is in the form of a step wedge and designed to measure accuracy and precision of AP bone mineral density (BMD) only. The more anthropomorphic Hologic spine phantom (Hologic, Waltham, MA) is similarly designed for assessment of AP BMD and, although when viewed laterally has the appearance of normal vertebrae, the components are of uniform density and would not provide a clinically representative image for morphometric analysis. Also, only four vertebrae (L1 to L4) are represented in the phantom. The European Spine Phantom simulates only L1 to L3 [9] and Felsenberg et al. [8] found the image quality obtained not entirely suitable for morphometry. All three of these phantoms have insufficient vertebrae for a full MXA procedure.

A phantom for use in MXA should be constructed of materials with similar attenuating properties to bone and soft tissue at the X-ray energies used. The design of the phantom should reflect clinically observed vertebral shape and range of deformities. It should enable validation and monitoring of the dependent parameters for MXA. These include mechanical parameters such as the alignment of the X-ray tube and detector, rotational position and longitudinal movement of the C-arm and registration of the image. Misalignment of the X-ray tube, in addition to affecting image quality, may result in the X-ray beam becoming non-parallel to the endplates of the vertebrae. This would result in an overestimate of vertebral height on morphometric images. The same effect would occur with misalignment of the C-arm relative to the central axis of the bed. If alignment changes with time, it may affect longitudinal assessment of vertebral deformity. Changes in the speed of movement of the C-arm during the scan procedure or in the system's image registration could result in misdiagnosis of vertebral collapse. For example, if the synchronization ratio between image position and actual position is correct at the beginning of the scan (1:1) but changes during the scan to a ratio of 1:2 at the end, then the thoracic vertebrae will appear foreshortened by a factor of 2.

Reproducibility of bed height should have minimal effect on vertebral height assessment but may result in distortion of the vertebral shape relative to a previous scan. Finally, in cases of vertebral deformity, accuracy confirmation is required, i.e., that the degree of wedging or collapse determined from the anterior/posterior or anterior/middle height ratios correlates with the true values.

Materials and Methods

Design

The phantom consists of three components: two aluminum and Perspex insert columns and a Perspex block with a drilled core (Fig. 2). The columns are constructed of 12 cylinders of aluminum, with phosphor-bronze endplates and a Perspex core, interspersed with Perspex disks. Aluminum was chosen for its bone-equivalent attenuation properties at the X-ray energies used and phosphor-bronze for its higher density and machinability to achieve thin endplates. Sharply defined endplates are required to maximize image clarity for the assessment of precision. The thicknesses of aluminum and phosphor-bronze were determined experimentally to give a similar morphometric image appearance as seen clinically.

The first column (column 1) is designed to check alignment, positioning and mechanical movements of the bed and C-arm. The cylinders are of the same height, 28 (±0.05) mm, including the endplate thickness of 0.05 mm (±0.005 mm), and are separated by an 'inter-vertebral space' of 7 mm. The second column (column

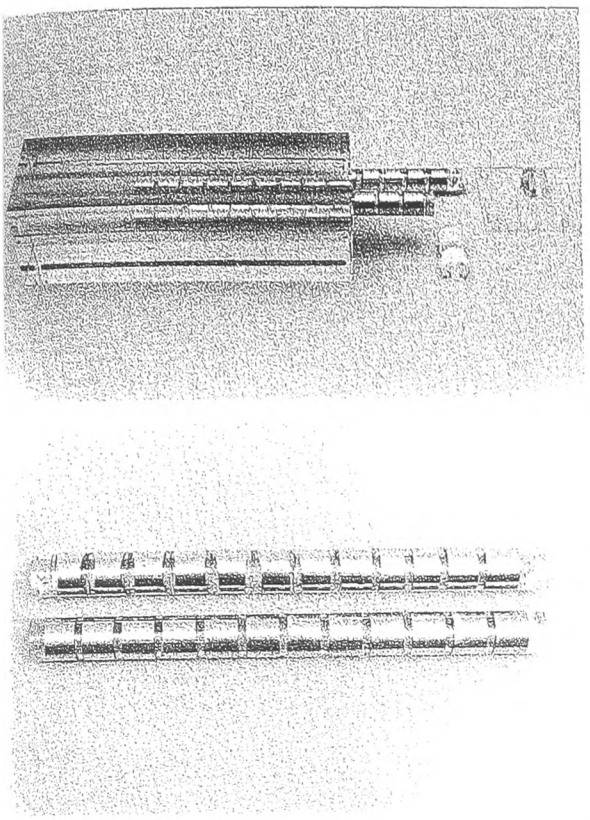

Fig. 2. a Phantom for use in morphometric X-ray absorptiometry. b Details of columns.

2) consists of three sets of cylinders: four of decreasing height, four of increasing anterior wedge and four of increasing biconcavity. The types and degree of deformities represent those found in the early stages of established osteoporosis, as described by others [2,10]. More severe deformities were not represented as diagnosis in these cases is generally beyond dispute. Each column may be inserted into the Perspex torso-mimicking block as required. Locating pins enable column 2 to be positioned at two predetermined angles relative to the plane of the X-ray beam, allowing the simulation of vertebral column rotation. All components of the phantom were carefully machined to ensure no air gaps, which could interfere with image quality by reducing X-ray attenuation in the 'soft tissue' regions.

The Perspex block incorporates radio-opaque markers at each end for monitoring X-ray beam alignment, C-arm position and bed height. An aluminum strip is incorporated posterior to the central core to simulate the posterior processes of the vertebrae.

Measurement

The phantom was placed along the central axis of the bed, mattress removed, with accurate positioning assured by aligning the locating markers with the positioning lines on the bed. Scanning was performed using the standard Lunar Expert-XL MXA acquisition with a bed height of –15 cm and scan length of 49 cm. Each column was scanned 10 times with repositioning between scans. Analysis was performed using the standard semi-automated MXA technique with manual adjustment of endplate markers as required, with points being longitudinally adjusted to the middle of the brightest pixel rows of the vertebral endplates, as currently recommended in the manufacturer's documentation. The scans were analyzed independently by two medical technical officers following the protocol recommended by the manufacturers. An image magnification of 300% was used to aid manual adjustment of the markers during analysis. To prevent fatigue errors, half the scans were analyzed from inferior to superior and half from superior to inferior.

Statistical Analysis

Analysis was performed using Microsoft Excel (version 5.0). Precision is expressed as percent coefficient of variation (CV %) with incorporation of RMS values for standard deviation [11]. Inter-operator variability was determined using Student's paired *t*-test, with a p value of less than 0.05 considered significant.

Results

The mean BMD of the 'vertebrae', assessed using a standard AP spine scan, was found to be 0.97 g/cm^2. MXA images of the two columns achieved with the Lunar Expert-XL are shown in Fig. 3. Using the semi-

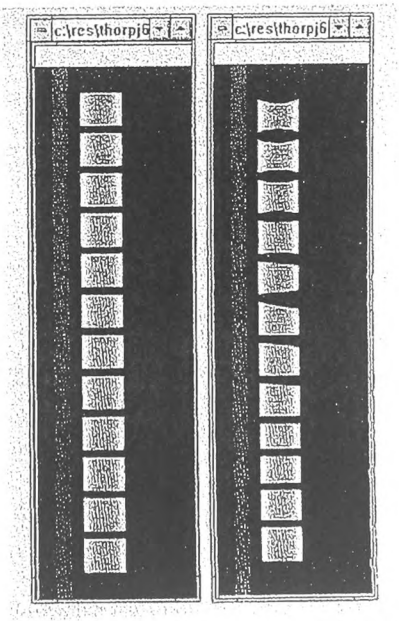

Fig. 3. Images of column 1 (left) and column 2 (right) obtained using the Lunar Expert-XL MXA.

automated analysis it was found that the software did not place the circular locating markers in the centre of the 'vertebrae'. The markers were generally placed anterior to the vertebrae and were incorrectly spaced, particularly in the upper part of the phantom corresponding to the thoracic region (Fig. 4). Manual adjustment was hence required to centralize the markers. The software then uses edge detection algorithms to locate the endplates and place identification points at the corners of each vertebra and in the centre of each endplate. Although the images are clearer than those often seen in clinical practice, the point placement was inaccurate and required manual adjustment to all 'vertebrae', again particularly in the 'thoracic' region. However, in our

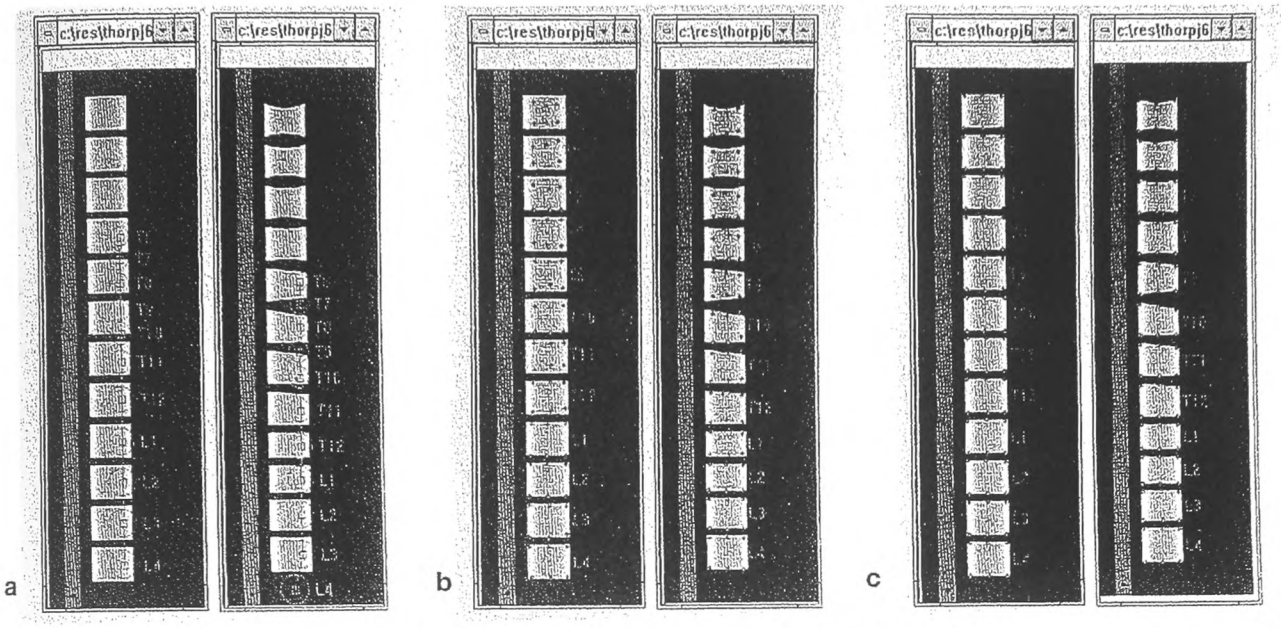

Fig. 4. Stages during MXA standard analysis showing: **a** automatic placement of circular locating markers, **b** subsequent automatic placement of endplate points and **c** Manually adjusted endplate points.

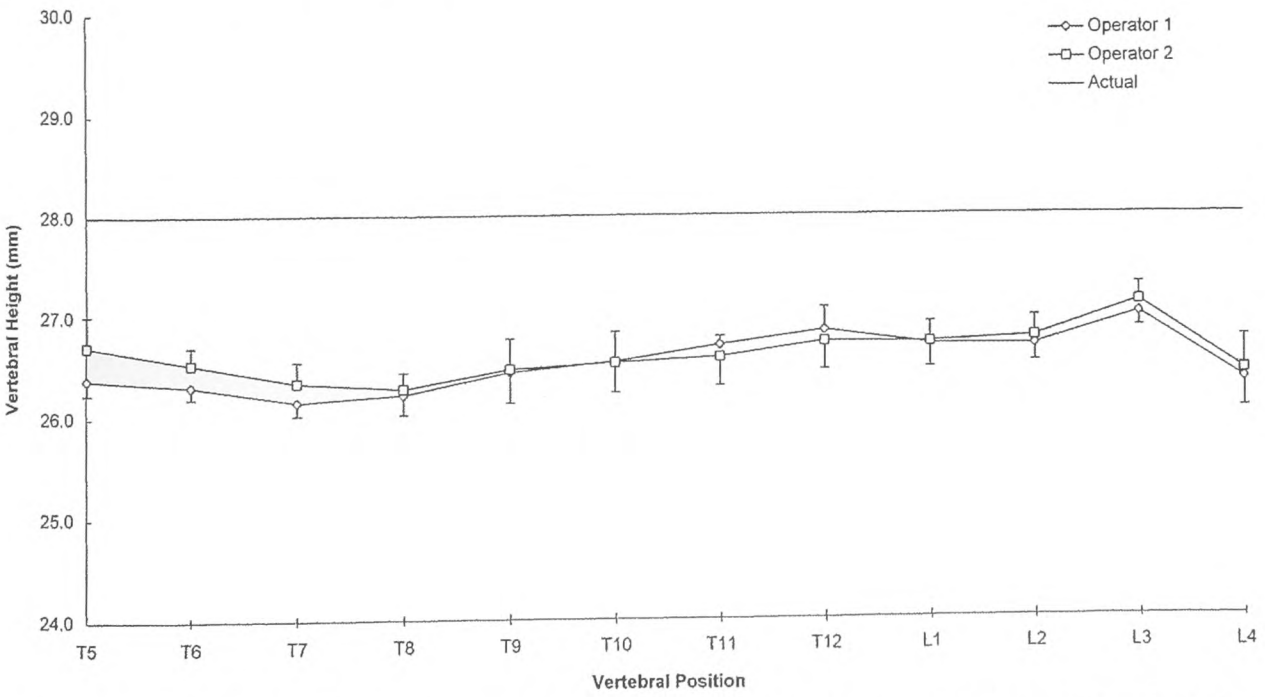

Fig. 5. Measured heights (mean ± SD) for each component of column 1 compared with actual heights. Results shown are the mean of anterior, middle and posterior heights from 10 scans performed using the Lunar Expert-XL MXA.

perience, the Lunar semi-automated analysis techni-
e makes similar errors with clinical images, frequently
sidentifying vertebrae and misplacing identification
ints.

The mean heights (anterior, middle and posterior) of
lumn 1 were on average 1.4 mm (4.9 %) ± 0.8 mm
is than the actual heights (Fig. 5). The height and
ecision of anterior, mid and posterior height for each
rtebra are shown in Table 1. There were few
gnificant differences in height assessment between
e operators for column 1, with those that were
served tending to be associated with the upper thoracic
rtebrae.

ble 1. Mean and precision (CV%) of measured heights determined each operator for column 1

	n	Operator 1	Operator 2	Mean difference
terior height				
	10	26.3 (1.08)	26.9 (1.15)	−0.56**
	10	26.5 (0.51)	26.4 (0.62)	0.09
	10	26.5 (0.70)	26.5 (0.65)	−0.06
	10	25.9 (0.95)	25.9 (0.75)	0.07
	10	26.8 (0.99)	26.6 (0.85)	0.19
0	10	26.5 (0.31)	26.3 (0.92)	0.16
1	10	26.8 (1.18)	26.6 (1.40)	0.27
2	10	26.9 (1.29)	26.5 (0.91)	0.37*
	10	27.1 (0.82)	27.1 (0.47)	−0.08
	10	26.4 (0.55)	26.5 (0.95)	−0.06
	10	27.1 (0.42)	27.2 (0.63)	−0.05
	10	26.5 (0.33)	26.5 (0.90)	0.03
verall	120	26.6 (0.83)	26.6 (0.88)	0.03
iddle height				
	10	26.4 (1.16)	27.1 (1.22)	−0.73**
	10	26.4 (0.57)	26.5 (0.70)	−0.05
	10	26.5 (0.75)	26.7 (0.99)	−0.15
	10	26.0 (1.07)	26.1 (0.83)	−0.04
	10	26.9 (0.99)	26.8 (1.38)	0.07
10	10	26.6 (0.33)	26.6 (1.40)	−0.02
11	10	26.9 (1.30)	26.8 (0.87)	0.12
12	10	27.0 (1.19)	26.7 (0.82)	0.30
1	10	27.2 (0.69)	27.3 (0.85)	−0.07
2	10	26.5 (0.55)	26.6 (0.87)	−0.06
3	10	27.2 (0.38)	27.2 (0.74)	−0.01
4	10	26.6 (0.80)	26.6 (1.45)	−0.06
verall	120	26.7 (0.87)	26.7 (1.04)	−0.06
osterior height				
5	10	26.4 (1.01)	26.7 (1.39)	−0.33*
6	10	26.3 (0.46)	26.5 (0.71)	−0.22*
7	10	26.2 (0.37)	26.3 (0.60)	−0.19**
8	10	26.2 (0.59)	26.3 (0.74)	−0.06
9	10	26.4 (0.54)	26.5 (0.84)	−0.03
10	10	26.5 (0.36)	26.5 (0.82)	0.01
11	10	26.7 (0.75)	26.6 (0.53)	0.12
12	10	26.8 (0.83)	26.7 (0.31)	0.11
1	10	26.7 (0.64)	26.7 (0.39)	−0.02
2	10	26.7 (0.37)	26.8 (0.50)	−0.08
3	10	27.0 (0.49)	27.1 (0.49)	−0.12
4	10	26.3 (0.37)	26.4 (1.03)	−0.09
Overall	120	26.5 (0.60)	26.6 (0.75)	−0.08**

The actual anterior, middle and posterior heights in all cases is 28 mm. The phantom was scanned 10 times with repositioning on a Lunar Expert-XL and analyzed using semi-automated MXA analysis
*$p<0.05$; **$p<0.01$ using paired t-test.

For column 2, expected ratios were calculated for each of the deformities. The degree of crush deformity was determined as a ratio of the posterior height to the mean measured height of L4 (non-compressed), for wedge deformities as anterior/posterior height and for biconcave deformities as middle/posterior height. The crush deformities (L4 to L1) were generally overestimated by 2% and the wedge deformities underestimated by 2%. On average, biconcavity was underestimated by 8% (Fig. 6). Mean and precision of measured heights for column 2 are shown in Table 2. There was found to be an increase in inter-operator variability, as would be expected, with the increased complexity of shape. Several significant

Table 2. Mean and precision (CV%) of measured heights determined by each operator for column 2

	n	Actual	Operator 1	Operator 2	Mean difference
Anterior height					
T5	10	28.0	24.5 (0.84)	24.5 (0.98)	0.00
T6	10	28.0	24.5 (0.77)	24.8 (0.94)	−0.31*
T7	10	28.0	25.2 (0.84)	25.3 (0.95)	−0.08
T8	10	28.0	24.9 (0.91)	25.2 (0.75)	−0.22*
T9	10	21.0	19.2 (1.04)	19.6 (1.09)	−0.39**
T10	10	22.4	20.0 (0.76)	20.5 (1.03)	−0.46**
T11	10	23.8	21.8 (0.76)	22.2 (1.98)	−0.41*
T12	10	25.2	23.4 (1.03)	23.8 (0.68)	−0.35**
L1	10	21.0	19.5 (0.64)	19.5 (0.65)	−0.07
L2	10	22.4	21.5 (0.53)	21.5 (0.88)	−0.06
L3	10	25.2	23.7 (0.53)	23.9 (0.68)	−0.20**
L4	10	28.0	27.0 (0.44)	27.1 (0.43)	−0.15*
Overall	120	25.1	22.9 (0.78)	23.2 (0.99)	−0.23**
Middle height					
T5	10	21.0	20.2 (0.71)	20.3 (1.42)	−0.02
T6	10	22.4	21.6 (0.90)	21.5 (1.05)	0.04
T7	10	23.8	23.0 (1.12)	23.2 (1.23)	−0.18
T8	10	25.2	23.7 (0.36)	23.7 (1.04)	0.01
T9	10	24.5	21.7 (1.11)	22.0 (1.09)	−0.30*
T10	10	25.2	22.1 (0.67)	22.2 (1.08)	−0.08
T11	10	25.9	23.6 (0.63)	23.8 (0.80)	−0.26**
T12	10	26.6	24.4 (0.64)	24.6 (1.50)	−0.21
L1	10	21.0	19.4 (0.50)	19.7 (1.30)	−0.22*
L2	10	22.4	21.6 (0.45)	21.6 (0.70)	−0.00
L3	10	25.2	23.7 (0.40)	23.9 (0.86)	−0.17*
L4	10	28.0	27.2 (0.59)	27.2 (0.36)	0.07
Overall	120	24.3	22.7 (0.72)	22.8 (1.08)	−0.11**
Posterior height					
T5	10	28.0	24.4 (0.59)	24.7 (1.48)	−0.27
T6	10	28.0	24.6 (0.38)	24.9 (1.07)	−0.34**
T7	10	28.0	24.8 (0.47)	25.1 (0.75)	−0.26**
T8	10	28.0	24.8 (0.50)	25.2 (0.82)	−0.37**
T9	10	28.0	24.8 (0.43)	25.2 (0.81)	−0.46**
T10	10	28.0	24.9 (0.46)	25.4 (0.72)	−0.50**
T11	10	28.0	25.2 (0.56)	25.6 (0.55)	−0.43**
T12	10	28.0	25.6 (0.87)	25.8 (0.81)	−0.22
L1	10	21.0	19.3 (0.60)	19.6 (0.92)	−0.29**
L2	10	22.4	21.3 (0.84)	21.5 (0.54)	−0.25**
L3	10	25.2	23.6 (0.45)	23.8 (0.62)	−0.25**
L4	10	28.0	26.9 (0.64)	27.0 (0.40)	−0.13*
Overall	120	26.7	24.2 (0.59)	24.5 (0.84)	−0.31**

Actual heights are given in the table. The column was scanned and analyzed as per column 1.
*$p<0.05$; **$p<0.01$ using paired t-test.

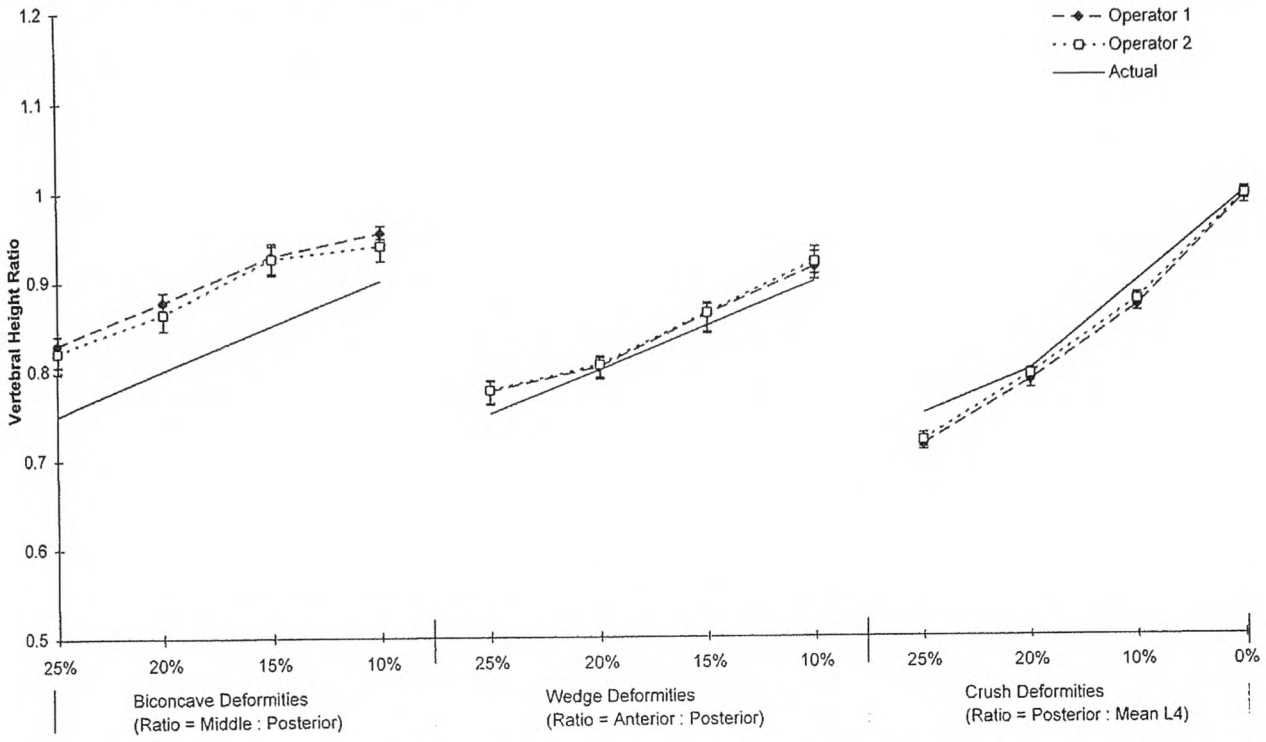

Fig. 6. Measured height ratios (mean + SD) form MXA of column 2 compared with actual: middle/posterior (biconcavities), anterior/posterior (wedges), posterior/posterior height L4 (crush).

differences were found in vertebral height measurement, particularly in posterior height assessment.

Discussion

A phantom has been designed that is suitable for determining the accuracy and precision of MXA vertebral height assessment and for monitoring long-term equipment stability. The phantom was designed for use on the Lunar Expert-XL but should be suitable for similar MXA machines and could provide a comparison with radiographic morphometric procedures. This is not a truly anthropomorphic phantom and has not been designed to validate the aspects of the proprietary software concerned with comparison to reference data. However, the phantom could be used to investigate inter-machine variability, which is a critical factor where reference data are to be accumulated or multicenter studies conducted.

The columns currently constructed have BMDs in the osteopenic range. MXA images obtained in osteoporotic subjects are generally of poorer quality, making analysis more difficult and reducing precision. However, the modular design of the phantom enables the construction and insertion of columns representing a range of densities and deformities, as found in clinical practice.

MXA of the phantom on the Lunar Expert-XL demonstrates incorrect placement of the circular locating markers by the semi-automated analysis. This suggests that the software is making assumptions about the shape of the vertebral column and relative dimensions of the vertebrae. Once the markers are manually adjusted to the correct location, the edge detection process places the endplate markers. The well-defined vertebral endplates on the image enabled accurate manual adjustment of the points where required.

Measurement of anterior, posterior and middle vertebral heights was consistently underestimated. This differs from the findings of Felsenberg et al. [8], who reported a mean overestimation of about 1.7% in vertebral height assessment on the Lunar Expert from MXA images of the European Spine Phantom. This may have been due to different scattering properties of the materials, but is more likely due to a difference in the protocols for the positioning of vertebral marker points. The observed underestimation of vertebral height may not be clinically significant, as the degree of vertebral deformity is generally determined relative to the heights of L2 to L4. However, this may have implications for the establishment of reference data. Normative data established by radiographic technique would have to be appropriately scaled. If reference data were to be accumulated on MXA machines, it would be important to ensure the comparability of results both within and between systems.

Mean precision of vertebral height measurement in vitro was found to be 0.84%. Using the method described by the British Standards Institution [12], a change in vertebral height of 2.38% would be required in

er to be reliably detected. This represents a mean nge in vertebral height of 0.7 mm, which corresponds h the MXA image pixel size (0.7 mm × 0.5 mm) on Lunar Expert-XL.

ncreasing complexity of vertebral shape caused a rease in accuracy and an increase in inter-operator iability. In particular, placement of points at the ter of the endplate of a biconcavity was found to be st accurate, producing an underestimate of deformity. o, location of the center of a wedged component is jective and any AP displacement will directly luence height assessment.

The initial findings using this phantom suggest that the nar Expert-XL MXA technique provides a precise asure of vertebral height. Defined protocols for rphometric analysis may reduce operator variability. though the absolute heights are underestimated, this is t considered detrimental as it is the ratio of heights it defines the morphometric status. If reference data to be accumulated or multicenter studies conducted these machines, such a phantom may be required to ess inter-system performance and provide cross-ibration.

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A phantom based study on the effect of subject positioning on morphometric X-ray absorptiometry using the Lunar EXPERT-XL

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Abstract. Morphometric X-ray absorptiometry (MXA) relies on accurate measurement of vertical dimensions of vertebrae from a lateral perspective. Deviations resulting from scoliotic curvature or poor patient positioning produce distortions of visible vertebral dimensions and may lead to analysis error. This study utilized a phantom developed at this centre to assess the effect of vertebral malalignment on the accuracy of the MXA technique on the Lunar Expert-XL. Measured vertebral heights were found to be consistently underestimated by an average of 3.7%. Precision ranged from 0.79% for anterior height measurement to 1.03% for middle height measurement. Vertebral malalignment was investigated as the effect of rotation around the anteroposterior, lateral and superoinferior axes. Rotation around the lateral axis produced little discernible effect. However, superoinferior axial rotation showed a change of more than two standard deviations in the mid/posterior ratios of biconcave vertebrae at comparatively small angles of rotation. Anteroposterior axial rotation produced an increase in observed height at small angles of rotation, and a rapid decrease in vertebral height as rotation increased. The results suggest that whilst kyphosis or lordosis of up to at least 5.8° has a minimal effect on MXA, scoliosis of 4.6° or above produces a distinctive effect on the defining crush height ratios.

Osteoporosis is a degenerative bone disease resulting in increased porosity and thinning of bone. Individual trabeculae may erode sufficiently to cause perforation with the resultant loss of supporting trabecular structure, greatly reducing mechanical integrity. This leads to a significantly increased risk of fracture, particularly in bones with a high trabecular content and stress bearing role such as the femur, radius and vertebrae. Studies have shown that vertebrae are likely to be the first sites of osteoporotic related fracture [1] and, unlike those of the femoral neck or radius, only about one-third of affected individuals present for clinical attention [2].

Examination of vertebral shape rather than density allows the assessment of the prevalence of vertebral fracture, which can aid the interpretation of bone mineral density (BMD) results, so assisting the overall assessment of the degree of osteoporosis. Vertebral fractures can be qualitatively identified radiographically from a change in the vertebral shape but, without previous radiographs for comparison, identification must be made from a comparison with other vertebrae on the same radiograph. Vertebral morphometry provides a quantitative method of assessing vertebral shape.

Vertebral morphometry depends on reliable measurement of vertebral height at three positions on the vertebrae: anterior, middle and posterior; with each height calculated from defining points positioned by the operator. Ratios defining the shape of the vertebrae are derived from these heights. Wedge and biconcavity deformations are defined by the ratios of the anterior/posterior heights and the middle/posterior heights, respectively. Crush deformations are detected by comparison of the posterior vertebral heights with the posterior heights of reference vertebrae (normally the lumbar vertebrae). Typically, a 3 standard deviation (SD) [3] or a 20% [4] or greater reduction in a particular height ratio is classified as a fracture.

Vertebral morphometry may be performed by conventional radiographic means with an excellent resolution of approximately 0.1 mm [5]. However, the X-ray cone beam geometry produces images with both magnification and projection distortion, especially towards the edges of the film. The projection distortion gives the vertebral endplates an elliptical appearance that can make measurement awkward and therefore assessment of vertebral

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compression difficult. The reproducibility of the technique is also reduced by the difficulty of placing the patient in the decubitus position. Recent technological developments such as CT lateral scout scans may eliminate distortion and positioning problems, but at the expense of poorer resolution.

Vertebral morphometry may also be performed using the morphometric X-ray absorptiometry technique (MXA) provided on some dual X-ray absorptiometry (DXA) systems. The Lunar Expert-XL (Lunar Corporation, Madison, WI, USA) is an example of the latest generation of DXA imaging densitometers, utilizing an X-ray fan beam and an array of solid state detectors, mounted on a C-arm to enable lateral imaging. The Expert-XL is capable of producing fast and high resolution images (40 s and 0.6 mm) of the thoracic and lumbar spine with the patient lying supine. MXA has a good patient acceptability and a low patient dose, 71 μSv for the Lunar Expert-XL [6], compared with typically 800 μSv for a standard lateral radiograph of the lumbar and thoracic spine [7]. The use of a fan beam overcomes the longitudinal distortion produced by a cone beam; whilst the supine patient position prevents the lumbar sagging that sometimes causes distortion in conventional X-ray procedures.

The Lunar Expert-XL software provides semi-automated analysis of the MXA image. Initially, circular location markers are automatically placed as labels for the vertebral bodies, then the vertebral endplates are located by an edge detection algorithm. The software places three diamond shaped defining pointers on each vertebral endplate, one point at each end and a point in the middle. The operator is able to make adjustments at each stage, and once adjustments are complete, the MXA software provides a comparison with reference data and indicates position and type of vertebral deformity.

Vertebral morphometry and MXA depend on the accurate measurement of the vertical dimensions of vertebra from a lateral perspective. Deviation from this perspective may result in distortion of visible vertebral dimensions and hence produce an error in the image analysis. Deviations result from a combination of spinal curvature, such as scoliosis, and patient positioning. This could conceivably cause large deviations in measured vertebral heights, possibly leading to the misclassification of vertebral compression by the automated software. Little work has been conducted on the effect of such factors on MXA. This has been due in part to the lack of an appropriate phantom that would allow a methodical investigation on the effect of projection angle on the results of clinical investigation. This study utilized a recently developed phantom [8] to assess the effect of patient positioning and spinal malalignment on the accuracy of the MXA technique on the Lunar Expert-XL.

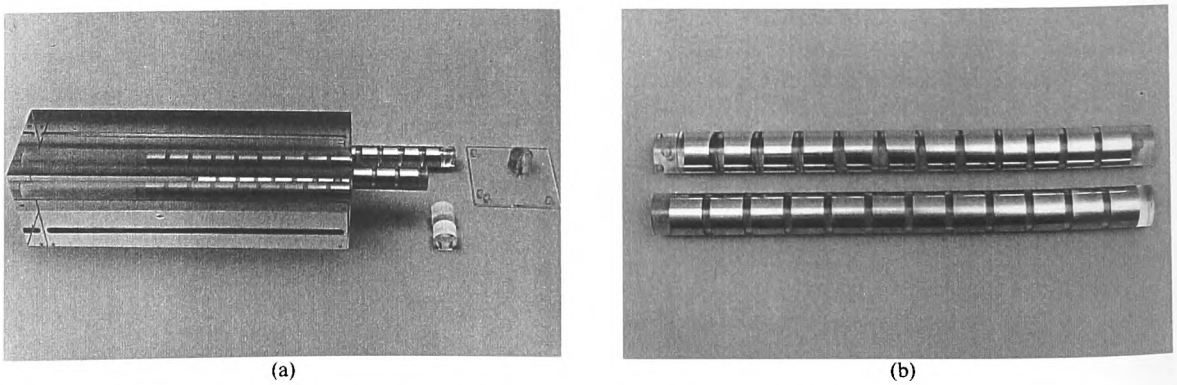
Method

Morphometry phantom

The phantom was developed in this centre to assess the accuracy and precision of MXA [8]. It consists of a Perspex block (15 cm × 15 cm × 50 cm), a drilled core and two interchangeable aluminium and Perspex columns (Figure 1). The Perspex block mimics the torso and the two columns mimic vertebrae of varying morphometric characteristics. Each column contains 12 artificial vertebral bodies, each constructed from a cylinder of aluminium, with a Perspex core and phosphor-bronze endplates. The artificial vertebrae of the first column (column 1) are all 28 mm high by 37 mm wide, representing the average dimensions of the lumbar vertebrae found in adult females. The 12 vertebral bodies of the second column (column 2) represent four varying degrees of crush, wedge and biconcavity fractures.

Simulation of vertebral rotation

The effect of vertebral malalignment on MXA was investigated by rotation of the phantom around three orthogonal axes (Figure 2). The



(a) (b)

Figure 1. (a) Phantom for use in morphometric X-ray absorptiometry. (b) Details of columns.

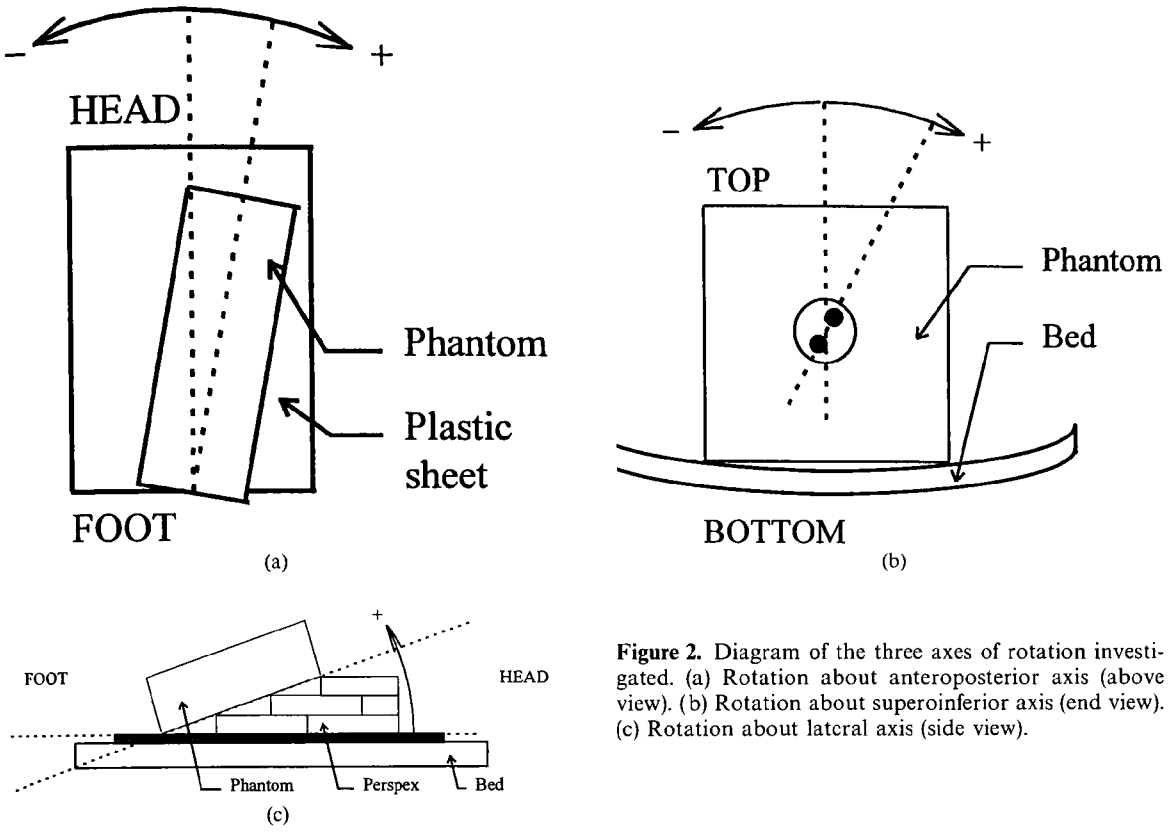


Figure 2. Diagram of the three axes of rotation investigated. (a) Rotation about anteroposterior axis (above view). (b) Rotation about superoinferior axis (end view). (c) Rotation about lateral axis (side view).

phantom was designed to be placed longitudinally on the bed, and rotation required the use of an underlying plastic board to correct for the lateral curvature of the scanning bed. For standardization, the sheet was used for all images and the mattress was removed. Positional reproducibility of ± 1 mm was achieved with the aid of location markers, the angle of rotation being calculated by trigonometry. The standard "lateral MM" acquisition mode was used throughout the procedure, with the longitudinal starting position of the C-arm set at 7.6 cm, the scan length at 46 cm and the bed height at -14 cm. Images were analysed immediately after acquisition, allowing sufficient time for the X-ray tube to cool ready for the next acquisition.

For calculation of accuracy and precision and provision of comparative data for the rotational images, each column was placed within the phantom block, with the block in an unrotated position. 10 images were then taken of each column, with repositioning between each acquisition.

For rotation around the anteroposterior axis, the Perspex block was positioned on the plastic sheet with the block turned sideways a set amount, measured by 1 cm markings placed on the sheet (Figure 2a). Imaging was conducted at 1 cm intervals between 0 and 7 cm and was repeated using both columns for both clockwise and anticlockwise rotation.

Only the wedged column was used for rotation around the superoinferior axis as the endplates of the straight column would always present the same profile to the X-ray beam. The wedged column was rotated both clockwise and anticlockwise within the phantom block, with imaging being conducted between 1 and 5 cm around the circumference of the bore of the block, at intervals of 1 cm (Figure 2b).

Rotation around the lateral axis was achieved by the elevation of the superior end of the phantom with Perspex sheets of known thickness. Additional Perspex was placed in the underlying airspace to prevent artefact. Imaging was conducted with both columns at elevations of 1–5 cm and increments of 1 cm (Figure 2c).

Image analysis protocol

MXA images of the two columns are shown in Figure 3. In the clinical situation, images are individually adjusted to optimize the display for analysis, thus the manufacturer (Lunar Corporation) does not give recommended display parameters. However, as this was a phantom investigation, a more rigid protocol was adopted to help standardize the procedure and minimize operator error. For analysis, the upper and lower values of displayed pixels were adjusted, so that edges of the vertebral bodies resolved as only single column thickness of white (maximum value) image pixels. For our system, this corresponded to upper and lower values of 6275 and 8000, respectively, with

Figure 3. Images of column 1 and column 2 obtained using Lunar Expert-XL MXA.

pixels below this range displayed as black, and those above displayed as white. Brightness and contrast modification controls were both set to zero. The homogeneity of the phantom gave a narrower range of pixel values; clinical images typically cover a wider range of around 4000 to around 14 000.

Images were displayed on a 54 cm Dell monitor and analysed under subdued lighting conditions by a single operator. To prevent fatigue from affecting operator variability during analysis, successive images were alternately examined from the top of the image to the bottom and from the bottom of the image to the top.

Following the manufacturer's recommendations, the circular location markers were manually adjusted into position over the centre of the vertebral bodies, with extra markers added if required. The positions of the defining pointers were also adjusted where required. For point adjustment, a more rigid protocol was used than that recommended by the manufacturer, which simply stated that marker points should be placed at the four corners of the vertebrae, and on the middle of the endplates.

Pointers were adjusted at maximum image magnification (500%) and positioned centrally on the brightest image pixels at the posterior, middle and anterior of each endplate. Where rotation of the phantom caused more than one edge of the same endplate to be visible, the mid-endplate pointers were positioned at the point of maximum separation, halfway between the two visible edges of the endplate (Figure 4).

Results

From the 10 control scans for column 1, the mean posterior vertebral height at zero rotation was found to be 26.9 mm ($\pm$0.21) giving a precision of 0.8%. This height was 1.1 mm less than the actual mean vertebral height of 28 mm. Similarly, for the middle and anterior measurements, the mean heights were 27.2 mm ($\pm$0.28) and 26.8 mm ($\pm$0.25), respectively; 0.8 mm and 1.2 mm less than the actual. A similar underestimation was observed for the individual vertebral heights of column 2.

For column 2, the calculated posterior/predicted posterior ratios for the crushed vertebrae were overestimated by an average of 1.0%, based on a predicted posterior height calculated from the mean posterior heights of L2 to L4 of the 10 control scans of column 1. The anterior/posterior ratio of the wedged vertebrae and the mid/posterior of the biconcave vertebrae was on average underestimated by 1.3% and 6.2%.

On a vertebral by vertebral basis, there was a slight variation in the measured heights along the length of column 1. A linear regression fit ($r^2 = 0.698$) showed a trend of increasing posterior

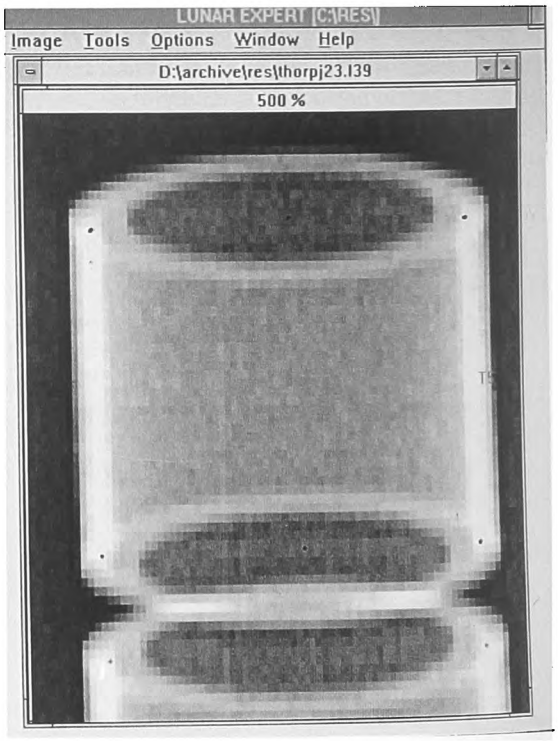


Figure 4. Enlarged image of rotated vertebral body from column 1 showing position of defining pointers.

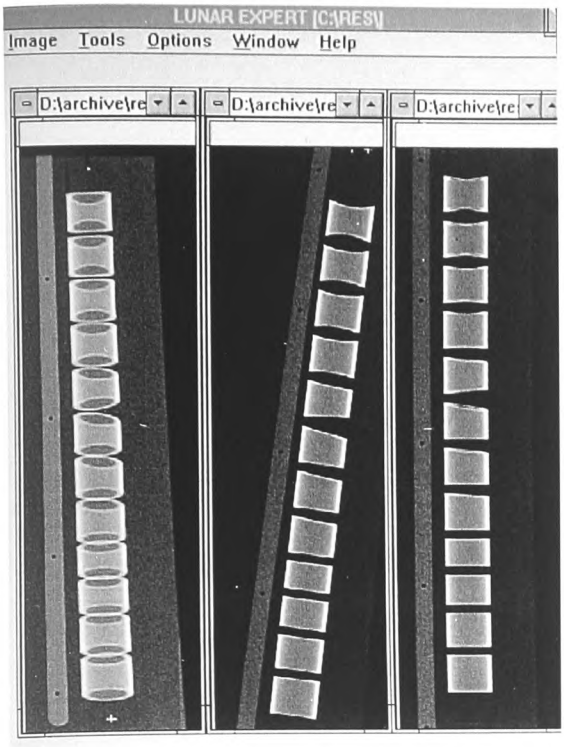


Figure 5. Images of column 2 at maximum angles of rotation. Left: at +15.8° rotation around the anteroposterior axis. Centre: at +5.9° rotation around the lateral axis. Right: at +23.0° rotation around the superoinferior axis.

height from T5 to L4, with the mean L4 being 0.64 mm (2.3%) greater than the mean T5.

Figure 5 shows images of column 2 at maximum positive angles of rotation for each of the three axes (anteroposterior, lateral and superoinferior). The effect of increasing anteroposterior axial rotation on the mean measured height for the three defining vertebral dimensions (posterior, middle and anterior) of column 1 is shown in Figure 6.

Anteroposterior axial rotation produced a clear effect on the measured vertebral heights of column 1. With positive rotation, vertebral height initially increased, reaching a mean peak of 27.9 mm at 4.6° before falling back to 25.7 mm at 15.8°. Negative rotation produced a similar effect for the posterior and anterior heights, reaching a peak at an average of 28.0 mm at −2.3°, but the middle height initially dropped to 26.5 mm at −2.3° before reaching a peak of 27.9 mm at −4.6°.

Rotation of column 2 showed a similar trend to that seen with column 1, with the mean heights increasing with small angles of rotation, before decreasing at larger angles. The middle measured height also showed a corresponding drop at −2.3°.

The effect of rotation around the anteroposterior axis on the defining vertebral ratios for column 1 and column 2 are shown in Figures 7 and 8. The observed change in vertebral heights produced variation in both posterior/predicted posterior ratios and the mid/posterior ratios, but little variation in anterior/posterior ratios. These effects were observed for both deformed and non-deformed vertebrae, as was the very sharp drop in the mid/posterior ratio at −2.3°.

Rotation of a column of vertebral bodies around the anteroposterior axis changes both the projection angle and the distance from individual vertebrae of the column to the X-ray source. Those vertebrae farthest from the point of rotation would be displaced by the greatest distance. If the distance from the vertebrae to the source produced the observed effect on measured vertebral height, the visible heights of those vertebrae farthest from the point of rotation would change more than those closer to the point of rotation. Examination of the data on a vertebra-by-vertebra basis showed that this was not the case. Thus source distance was not a factor in the observed change in vertebral height.

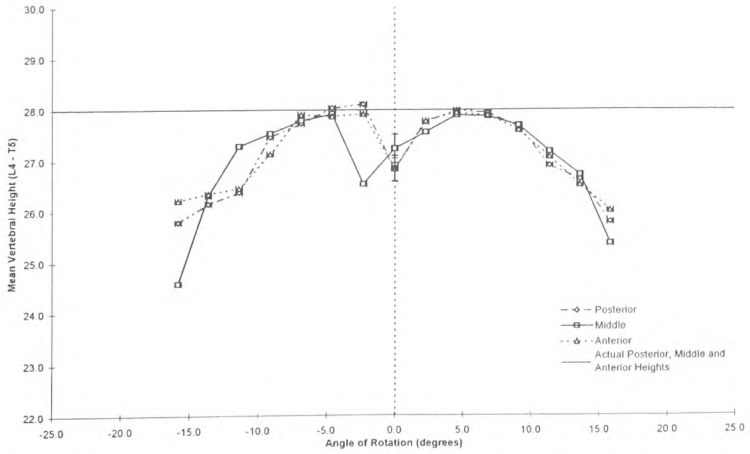


Figure 6. Variation in posterior, middle and anterior mean vertebral heights with rotation of column 1 around the anteroposterior axis, with actual values as comparison. Mean heights and standard deviations at zero rotation calculated from 10 control scans. Angular error calculated assuming a ±1 mm positional inaccuracy.

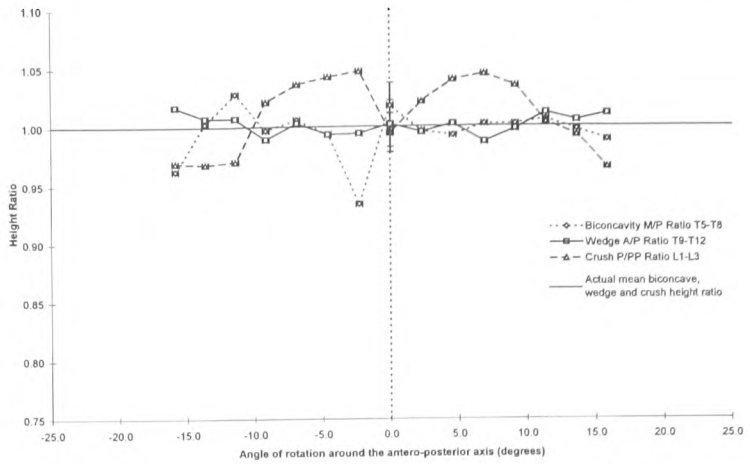


Figure 7. Variation in defining ratios for biconcave, wedge and crush deformities with anteroposterior axial rotation of column 1, with actual values as comparison. Ratio error at zero rotation calculated from control scans assuming ± 1 SD in both numerator and denominator. Angular error calculated assuming a ± 1 mm positional inaccuracy.

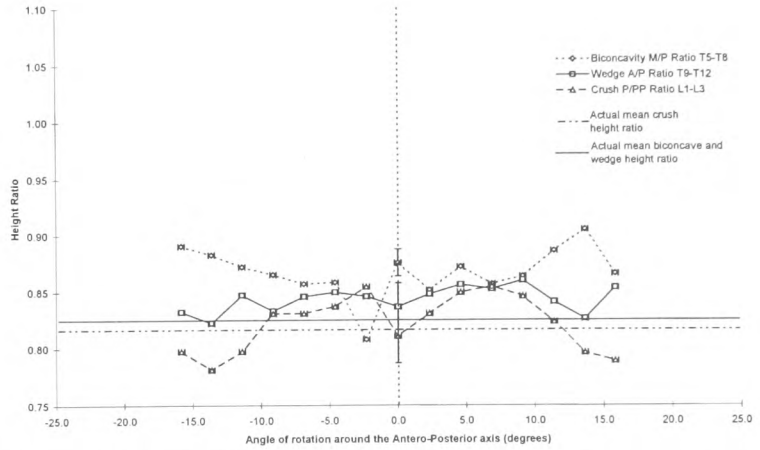


Figure 8. Variation in defining ratios for biconcave, wedge and crush deformities with anteroposterior axial rotation of column 2, with actual values as comparison. Ratio error at zero rotation calculated from control scans assuming ± 1 SD in both numerator and denominator. Angular error calculated assuming a ± 1 mm positional inaccuracy.

Increasing angles of rotation of both column 1 and column 2 around the lateral axis produced only slight deviations in the mean vertebral heights from the unrotated means. At the maximum angle of rotation of 5.9° degrees, the posterior, middle and anterior heights varied from the unrotated heights by only -0.24, $+0.26$ and $+0.05$ mm for column 1 and $+0.02$, $+0.22$ and $+0.45$ mm for column 2, respectively. Taking into account the respective standard deviations of operator error of ± 0.21, 0.28 and 0.25 mm for column 1 and ± 0.26, 0.23 and 0.33 mm for column 2, only the posterior height of column 1 and the anterior height of column 2 deviated from the average by more than 1 SD, and no mean height varied by more than 2 SD.

Correspondingly, all defining vertebral ratios calculated from the anterior and posterior vertebral heights of column 2 were within 2 SD of those expected. There was no systematic error in the results associated with degree of deformity. All other defining ratios, including all of those calculated for column 1, were within 1 SD of those expected.

The effect of positive and negative rotation around the superoinferior axis produced little visible effect on the combined mean heights of vertebrae in column 2. However, separate examination of the defining ratios for the three types of vertebral deformity revealed that there was some pattern of variation, as shown in Figure 9. From this it can be seen that crushed and wedged vertebrae showed almost no variation with rotation, but biconcave vertebrae showed a noticeable change in the defining mid/posterior ratio, although with no clear pattern. The change in the ratio exceeded 2 SD at $+9.8°$ and $-4.9°$ and 1 SD at $+4.9°$ and $-9.8°$ but was less than 1 SD at $\pm 14.5°$ or more. Additionally, the effect did not appear to increase with the increasing severity of biconcavity.

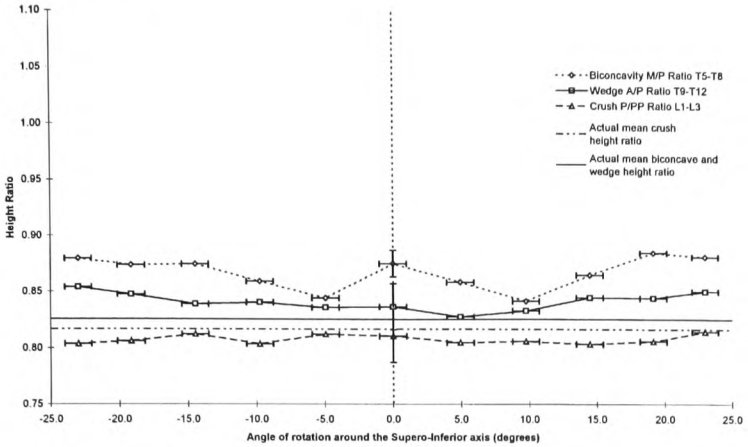


Figure 9. Variation in defining ratios for biconcave, wedge and crush deformities with superoinferior axial rotation of column 2, with actual values as comparison. Ratio error at zero rotation calculated from control scans assuming ± 1 SD in both numerator and denominator. Angular error calculated assuming a ± 1 mm positional inaccuracy.

Discussion

Vertebral morphometry relies upon accurate assessment of vertebral height from a lateral perspective. Deviation from this perspective can produce a change in the projected image, with such deviations potentially occurring through poor patient positioning or spinal deformity. Until now, little work has been carried out to measure the effect of poor positioning, but the MXA phantom developed at this centre has allowed the systematic evaluation of the effect of such positional errors on the results of MXA examination.

The phantom was designed with a BMD within the osteopenic range (0.97 g cm^{-2}). Also, the phantom vertebral components provide more clearly defined endplates than might typically be seen with actual vertebrae, so the actual *in vivo* precision of osteopenic and osteoporotic subjects is likely to be less. It is also possible that operator error increases with the angle of rotation, but testing this would require a prohibitive number of repeat scans at each angle.

The underestimation of the mean vertebral heights of the phantom by the Lunar Expert-XL differed from the results of Felsenberg et al [5], who found that the earlier Lunar Expert overestimated vertebral height of the European Spine Phantom by about 1.7%. Although it is possible that this difference was due either to differences between the machines used, or to scatter differences between the two phantoms, it seems more likely that it was due to a difference in the image analysis protocols.

The unexpected upward trend in observed posterior vertebral height of around 0.64 mm from T5 to L4 was considerably larger than the mean operator variability, so was unlikely to be due to chance. Later investigation, with additional Perspex for attenuation, showed that this effect was probably due to accumulating saturation of the detector as the acquisition progressed towards T5. Increasing the thickness of the Perspex used to 25 cm eliminated the upward trend in vertebral height. A phantom of this size would be impractical, but additional Perspex may be added prior to use. The reduction in vertebral height due to detector saturation would be unlikely to produce an effect on the results of this investigation as the saturation would be present in all images. However, the lack of visible distortion in the individual images does demonstrate the insidious nature of detector saturation, and care should therefore be taken to reduce it in both the *in vivo* and *in vitro* application of MXA.

The effects of rotation around the three primary axes: anteroposterior, superoinferior and lateral, were investigated. It was expected that rotation around the anteroposterior axis would follow a simple cosine relationship between the angle of rotation and the vertebral height. From the results it could be seen that this was not the case, as the mean vertebral height increased with small angles of rotation, before decreasing at a more expected rate for a cosine function. In the images, small angles of rotation caused displacement of the proximal and distal edges of the endplate sufficient to show a double thickness of pixels but insufficient to resolve them separately. The presence of an extra row of pixels on each endplate effectively increased the measured vertebral height by their combined thickness. As the longitudinal resolution of the Lunar Expert-XL is 0.7 mm, the potential height increase would be about 1.4 mm, which was as observed. If this supposition were correct, a similar result would be expected clinically.

An exception to this occurred at $-2.3°$ of anteroposterior rotation. At this point, one row of bright pixels at each endplate was slightly darker than

the other, causing the operator to reposition the mid points accordingly. This might explain the sharp drop in the observed middle heights at that angle of rotation. If so, the resulting drop in the measured height can be dismissed as an artefact produced by the rigid image analysis protocol.

As rotation had a similar effect on the anterior, middle and posterior vertebral heights, the mid/posterior and anterior/posterior ratios varied only slightly; although the mid/posterior ratio at $-2.3°$ was an exception to this owing to the previously described effect. The crush ratio, however, depends on a comparison of the posterior height with a predicted posterior height and as such was seriously affected by rotation, with a significant deviation in the ratio at only $\pm 4.6°$ of rotation. The Lunar software corrects for this by using the measured heights of L2–L4 for calculating the predicted height. Hence, if the subject was positioned with the whole spine at one angle of rotation, the predicted posterior height would be reduced by a similar amount to the other individual posterior heights. However, a scoliosis can produce anteroposterior rotation of only a limited area of the spine, making correction ineffective in these cases. It therefore follows that at greater than $\pm 4.6°$ of anteroposterior (scoliotic) rotation, the posterior/predicted posterior ratio for detecting crush fractures is unreliable and so the use of MXA in such cases is questionable.

It was found that, as expected, superoinferior rotation did not produce any effect on the vertebral heights of the crushed vertebrae L1–L4, greater than that explicable by 1 SD of operator error. Unexpectedly, the same was also found to be true for the wedged vertebrae T12–T9. However, significant changes of greater than 2 SD in vertebral height were observed for the biconcave vertebrae of T5–T8 at some angles of rotation.

Superoinferior rotation corresponds to twisting of the vertebral body and could have an anatomical or positional cause. This study has shown that the diagnosis of biconcavities can be affected by small angles of rotation, and caution should therefore be taken to ensure that the patient is lying anatomically supine prior to imaging.

Vertebrae rotated around the lateral axis appear diagonal in the image, with some of the vertebral height expressed as width (see Figure 5). The Lunar Expert-XL software automatically compensates for this by calculating the diagonal height. However, the lateral fan geometry of the X-ray beam causes a magnification of the width of an object, with the degree of magnification increasing with distance from the centre of the beam. In practice we found that rotation around the lateral axis had little discernible effect on either the measured vertebral height or the ratios for either column. The results therefore suggest that any angle of kyphosis or lordosis of up to 5.8° would not produce any significant change in vertebral height.

The observed changes were proportional to the overall vertebral height, so results of rotation should be applicable to all patient sizes. However, the phantom used in this study is not truly anthropomorphic, so caution should be taken in applying the results of this investigation to the clinical situation.

In view of the detector saturation observed in this investigation, care should be taken during clinical acquisitions to reduce to a minimum the number of unattenuated photons reaching the detector. The tube current selected should therefore be appropriate for the amount of soft tissue present in the target area, whilst for lateral acquisitions, an appropriate bed height should be ensured to reduce the airspace above and below the subject in the resultant image.

Overall, these results demonstrate that great care should be taken to align the patient along the central axis of the scanning couch. This could be achieved with the aid of the positioning laser and confirmed with an anteroposterior spine scan. Additionally, the application of the MXA technique becomes questionable in scoliosis of above 4.6°, but can compensate for degrees of kyphosis or lordosis of up to at least 5.8°. Care should therefore be taken to distinguish and exclude scoliotic vertebrae from the results of any MXA examination.

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The DXL Calscan heel densitometer: evaluation and diagnostic thresholds

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ABSTRACT. The DXL Calscan (Demetech AB) is a new dual energy X-ray absorptiometry device for determining heel bone mineral density (BMD). The system is based on the standard technique of dual energy X-ray absorptiometry (DXA), using a fan beam configuration, but introduces an additional laser measurement of heel thickness intended to improve accuracy. We have examined the utility, *in vitro* and *in vivo* performance of the DXL Calscan and established triage thresholds based on the UK's National Osteoporosis Society guidelines on peripheral densitometry. The Calscan proved convenient, easy to use and was stable over time and within a range of operating temperatures. Short-term *in vitro* precision as %CV, with phantom repositioning, was 0.75% and long term precision 0.73%. Precision *in vivo*, determined from duplicate right heel scans of 67 subjects, was 1.19%. Effective radiation dose to the patient was <0.1 μSv per scan. 140 white females (70 osteoporotic and 70 non-osteoporotic), aged 55–70 years underwent scans of both heels. Subjects were defined as osteoporotic or non-osteoporotic on the basis of axial DXA (spine L2–L4 and total hip). Triage thresholds for reassurance-referral or referral-treatment were 0.391 g cm^{-2} and 0.306 g cm^{-2} for non-dominant and 0.395 g cm^{-2}, 0.294 g cm^{-2} for dominant heel, respectively. The non-dominant heel proved slightly superior to the dominant for triage purposes. Of the seven non-osteoporotic subjects misclassified as osteoporotic by Calscan of either heel, six had severe axial osteopenia. If operated by trained personnel and used in appropriate populations exhibiting risk factors, the Calscan is well suited for use in the management of post-menopausal osteoporosis.

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Measurement of bone mineral density (BMD) by dual energy X-ray absorptiometry (DXA) is now well established as the method of choice for osteoporosis assessment [1–3]. BMD assessment of the lumbar spine and hip by DXA represents the current gold standard due to the greater associated morbidity and mortality of fractures at these two sites, superior fracture prediction [4, 5] and response to treatment [6]. In addition to axial assessment, there are a variety of DXA devices available for measuring BMD in the forearm, heel and hand.

The DXL Calscan (Demetech AB, Solna, Sweden) is a new peripheral device for calcaneal BMD assessment, based on fan beam DXA. The Calscan also incorporates a laser measurement of heel thickness to improve the accuracy of calcaneal BMD. Standard DXA assumes a two compartment model of tissue masses, the first bone and the second a composite of lean and adipose tissue at an assumed constant ratio. This assumed ratio does not allow for fluctuations in lean and adipose tissue proportions that have been demonstrated to occur at the spine [7] and are likely to occur at the calcaneus or elsewhere [8, 9]. This leads to calcaneal DXA providing a precise but potentially inaccurate estimate of BMD, with the degree of inaccuracy dependent on body mass index [8].

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These inhomogeneities can be corrected by solving the BMD equation as a three component model of bone, lean and adipose tissue. Swanpalmer [10, 11] described how a third X-ray energy could achieve this, but concluded that a significantly higher photon count (and hence scan times) would be required to maintain an acceptable degree of precision.

Jonson [12] deduced that if the combined width of all three components were known, *e.g.* the width of the heel, the ratio of soft to lean tissue could then be derived and corrected for. The laser heel width measurement on the Calscan provides this additional dimension allowing the derivation of BMD from a three component model, whilst theoretically maintaining DXA precision [13].

As with other peripheral DXA (pDXA) devices [14], the Calscan is smaller, portable, cheaper and has a lower radiation dose than axial densitometers. However, pDXA results at the calcaneus cannot be interpreted using the WHO definition [15] and do not correlate perfectly with bone density at either spine or hip. The imperfect correlation can lead to pDXA misclassifying subjects to the opposite diagnostic group to which they would have been classified by axial DXA [16–18], particularly for subjects with BMD scores close to diagnostic thresholds. Hence considerable debate remains over how such peripheral devices might best be employed in the clinical setting. The UK-based National Osteoporosis Society (NOS) has recently stated

that current evidence supports the use of peripheral devices in a triage rather than diagnostic role, and has established a method for determining the required triage thresholds [19, 20]. The aim of this study was to determine the *in vitro* and *in vivo* operating conditions of the Calscan and to establish triage referral thresholds based on the NOS guidelines.

Materials and methods

The DXL Calscan bone densitometer (Figure 1) utilizes a fan beam, dual energy X-ray source and a solid state detector to perform a scan of the heel. A region of interest is positioned automatically by the software to derive BMD. A concomitant measure of heel thickness is obtained using the laser reflection to correct for variations in the soft to lean tissue ratio. The Calscan, at 25 kg in weight and 80 cm long by 43 cm wide and 33 cm tall, is relatively compact and easy to transport and includes wheels at one end and a carry handle. As with all X-ray equipment, the Calscan is potentially subject to changes in tube temperature after performing an acquisition, and as a portable device it may also be subject to fluctuations in performance due to environmental changes. To counter this, the software (version 1.3.1) requires a warm-up acquisition when the device is switched on and a 4 min cooling down period after each acquisition.

In vitro methodology

Phantom based studies were conducted to test the effect of temperature, stability following relocation and to determine *in vitro* precision. The DXL-Calscan comes with a manufacturer-supplied phantom, made from shaped pieces of aluminium depicting the calcaneus, embedded in acrylic. Short term precision was determined as percent coefficient of variation (%CV) from 30 scans with phantom repositioning and 30 without. The device was operated according to the manufacturer's instructions. All measurements were taken on the same day. Accuracy was calculated from comparison with the phantom's stated BMD of 0.347 g cm^{-2}, established from a central reference machine, corresponding to a T-score of −2.1. Long term *in vitro* precision was determined using daily single phantom scans acquired over a period of 6 months as part of routine quality assurance.

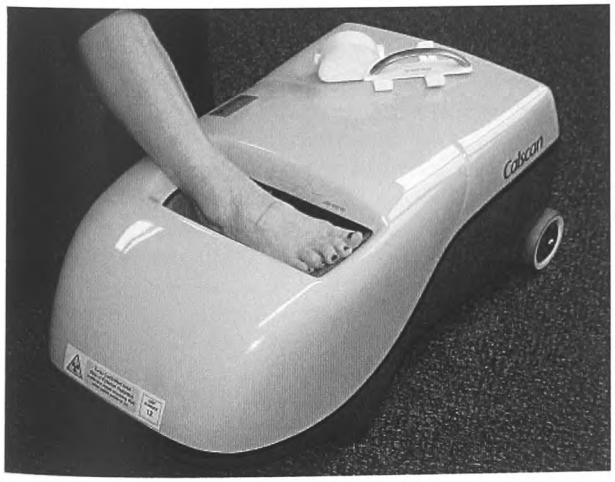

Figure 1. The Demetech DXL Calscan and phantom.

Sixteen tests were conducted to assess the effects of ambient temperature, device movement or tube heating on accuracy or precision. For each test the device was disconnected, moved to a different room, warmed up and a phantom scan acquired as soon as the warm-up was complete. The device was given a further 30 min to stabilize, then a second phantom scan was acquired and the device powered down and allowed to cool for 30 min before beginning the next test. Temperature was measured on an alcohol room thermometer throughout. Electrical, laser safety and radiological protection surveys were also carried out.

In vivo methodology

Subjects

Females attending for routine BMD of spine and hip were approached for participation in this study. These were referred on the basis of agreed local risk criteria which are broadly in agreement with those of the Royal College of Physicians [1]. The study was approved by the local research Ethics Committee and informed consent was obtained. All subjects were white and between the ages of 55 years and 70 years (Table 1). A total of 140 women were recruited.

Axial DXA assessment

Subjects underwent BMD of lumbar spine and hip using a GE-Lunar Prodigy (GE-Lunar, Madison, WI) as part of their routine examination and clinical management was determined on the basis of the results. In our centre, DXA of the right hip is performed unless contraindicated. For the purposes of this study, if the lower of either L2–L4 spine or total hip BMD T-score values was below −2.5, the subject was classified as osteoporotic. Otherwise they were classified as non-osteoporotic. When lumbar vertebrae showed clear signs of degenerative changes, the individual vertebrae affected were excluded from the lumbar spine results. Four subjects had individual vertebrae excluded – one osteoporotic and two non-osteoporotic subjects with degenerative changes of L4 and one non-osteoporotic subject with changes at L3. For eight other subjects (four osteoporotic, four non-osteoporotic by final diagnosis), two or more vertebrae on the same subject showed

Table 1. "Evaluation and Diagnostic Thresholds of the DXL Calscan". Mean (standard deviation) subject demographic variablesfor whole group, osteoporotic and non-osteoporotic subjects, respectively

	Whole group	Osteoporotic	Non-osteoporotic
n	140	70	70
Age (years)	62.7 (4.5)	63.2 (4.3)	62.2 (4.7)
Height (cm)	159.4 (6.5)	159.2 (7.0)	159.5 (6.0)
Weight (kg)	64.3 (10.7)	62.6 (11.1)	66.0 (10.1)
BMI (kg m^{-2})	25.3 (3.9)	24.7 (3.9)	26.0 (3.9)

BMI, body mass index.

degenerative changes. For these eight subjects the spine results were disregarded and diagnosis was made by total hip DXA alone. In one case this caused the subject to move from the osteoporotic to non-osteoporotic group. Recruitment continued until 70 osteoporotic and 70 non-osteoporotic subjects were enrolled.

Calcaneal DXA assessment

BMD of both heels was obtained using the DXL Calscan. To determine *in vivo* precision, 67 of the 140 subjects underwent a repeat acquisition of the right heel, with repositioning between each. The calcaneal regions of interest (ROI) were manually checked and, if deemed necessary, ROI position was corrected as per the user manual instructions. For the repeat Calscan acquisition, the second scan for each subject was analysed on a separate day to the first to reduce the possibility of operator bias during any ROI repositioning.

Results

Operational utility

The time from scan initiation to appearance of the results is 94 s, with an additional 4 min required to allow the X-ray tube to cool before another acquisition can be taken. The Calscan is able to image either heel from the same side of the device making it easier for the patient and minimizing floor space required where both heels are to be scanned. As for all equipment using ionizing radiation, the Calscan requires a standard radiation safety assessment but also an additional laser safety assessment. The footwell of the Calscan was of an open design, and had the advantage of allowing the operator to manually assist the positioning of the heel. The open design allowed easy access for the operator and was comfortable for the patient, but did require some attention to achieve the ideal positioning.

In vitro results and environmental effects

Short term *in vitro* precision (coefficient of variation) was 0.76% CV (mean BMD 0.347 ± 0.0026 g cm^{-2}) with phantom repositioning, 0.75% (0.347 ± 0.0025 g cm^{-2}) without. Long term precision was 0.73%. The device was accurate, with no measurable difference between mean phantom BMD as measured on our machine compared with that of the central reference machine.

Average phantom BMD and precision for the 32 environmental scans was 0.347 g cm^{-2} and 0.62% CV. Average phantom BMD and precision for the 16 scans taken as soon as possible after a warm-up scan, *i.e.* after the enforced 4 min cooling down period between scans, was 0.347 g cm^{-2} and 0.65% CV. For the 16 scans acquired after the tube had been allowed to cool for half an hour, average BMD was 0.348 g cm^{-2} and 0.61% CV.

During the 32 scans of the 16 environmental tests, the room temperature varied from 21.3℃ to 26.9℃, the upper value being slightly outside the manufacturer's recommended operating range of 15℃ to 25℃. Comparison of the results recorded at the 16 highest temperatures (range 23.8℃ to 26.9℃) with the results at the 16 lowest (21.3℃ to 23.8℃) did not change phantom BMD or precision significantly. For the 16 higher temperature scans, phantom BMD and precision was 0.347 g cm^{-2} and 0.64% CV, respectively. For the 16 lower temperature scans, phantom BMD and precision was 0.348 g cm^{-2} and 0.58% CV, respectively.

Radiation and laser safety

The effective radiation dose to the patient was <0.1 μSv per scan and a controlled area of 0.5 m was defined around the device in order to comply with IRR 1999 [21]. At this distance, scatter dose to the operator would not exceed annual dose limits, even at maximum scan throughput. The laser assessment found the Calscan laser itself to be class 2 by UK/European/US standards and thus capable of causing eye damage, but the location of the laser within the footwell removed the possibility of accidental exposure and so the laser was deemed to be safe (class 1), provided the Calscan outer casing was in place. The permanent filtration and laser class were not marked on the casing as is required to comply with UK/EU standards [22, 23]. A laser warning label was added to the Calscan and local rules were established that reflective objects should be kept clear of the footwell, as stated in the user manual. No other laser precautions were deemed necessary. No safety problems with the laser occurred during the project, but it was noticed that opaque black hosiery could produce spurious BMD results, although other hosiery did not.

In vivo results

Subject demographics and bone density results are summarized in Tables 1 and 2, whilst coefficients of determination (adjusted R^2) between key variables are shown in Table 3. Mean *in vivo* BMD of the right heel for all 67 subjects (19 osteoporotic, 48 non-osteoporotic) given repeat measurements was 0.357 g cm^{-2} (range 0.186–0.518 g cm^{-2}, standard deviation 0.074 g cm^{-2}). Mean absolute difference between paired results was 0.0046 g cm^{-2} (range 0–0.018 g cm^{-2}). Calscan precision for the 67 subjects as %CV (derived from root mean square) was 1.19%.

Taking the osteoporotic and non-osteoporotic precision groups separately, mean BMD for the 19 osteoporotic subjects was 0.299 g cm^{-2} (0.186–0.437 g cm^{-2}, SD 0.065). Mean absolute difference was 0.0042 g cm^{-2} (0–0.012 g cm^{-2}). Precision was 1.30%CV. For the 48 non-osteoporotic precision subjects mean BMD was 0.392 g cm^{-2} (range 0.281–0.518 g cm^{-2}, SD 0.061). Mean absolute difference was 0.0048 g cm^{-2} (0–0.0018 g cm^{-2}). Precision was 1.09%CV.

Establishing triage thresholds

In the revised NOS guidelines on peripheral DXA, Blake et al [20] recommend the use of peripheral devices in a triage role as an adjunct to axial DXA and suggest a

Table 2. "Evaluation and Diagnostic Thresholds of the DXL Calscan". Mean (standard deviation) DXA bone density and T-score results for whole group, osteoporotic and non-osteoporotic subjects, respectively

		Whole group	Osteoporotic	Non-osteoporotic
Spine L2–L4	BMD	0.948 (0.173)	0.822 (0.070)	1.076 (0.152)
	T-score	−2.10 (1.45)	−3.15 (0.59)	−1.03 (1.26)
Total hip	BMD	0.832 (0.122)	0.774 (0.092)	0.892 (0.121)
	T-score	−1.39 (1.02)	−1.88 (0.77)	−0.89 (1.01)
Non-dominant heel	BMD	0.356 (0.064)	0.328 (0.054)	0.383 (0.062)
	T-score	−1.96 (0.97)	−2.37 (0.82)	−1.53 (0.93)
Dominant heel	BMD	0.356 (0.064)	0.328 (0.050)	0.383 (0.065)
	T-score	−1.96 (0.97)	−2.38 (0.75)	−1.54 (0.99)

Units: BMD (g cm^{-2}); T-score (St Dev).
BMD, bone mineral density.

Table 3. "Evaluation and Diagnostic Thresholds of the DXL Calscan". DXA BMD Correlation (adjusted R^2 value)

	Spine L2–L4	Total femur	Dominant heel	Non-dominant heel
Spine L2–L4	1	0.379	0.285	0.276
Total femur		1	0.331	0.350
Dominant heel			1	0.905
Non-dominant heel				1

method for defining the two triage thresholds required. The upper of the two thresholds is set at a point above which only 10% of osteoporotic subjects would fall, whilst the lower threshold is a point below which only 10% of non-osteoporotic subjects would fall. Subjects who fall above the upper threshold would be assumed non-osteoporotic, whilst subjects who fall below the lower threshold assumed osteoporotic. Subjects falling between the two would be recommended for referral for axial DXA.

Using the 140 subjects in this study, the upper and lower thresholds for Calscan for the non-dominant and dominant heels are shown in Figure 2. The proportion of subjects in the equivocal group, and therefore requiring axial DXA, is shown in Table 4. Based on these thresholds of 0.391 g cm^{-2} and 0.306 g cm^{-2} for the non-dominant and 0.395 g cm^{-2} and 0.294 g cm^{-2} for the dominant heel, the referral rates for the Calscan in this group were 52.9% (non-dominant) and 58.6% (dominant), but with an error margin of ±9% due to the small sample size. Of the seven non-osteoporotic subjects misclassified as osteoporotic by Calscan of either non-dominant or dominant heels, six had severe osteopenia (axial T-score <-2).

A better estimate of the expected referral rate can be drawn from comparing our derived thresholds (and confidence intervals) to the mean and standard deviation of the Calscan reference data. The reference data are drawn from a population of 993 Swedish women between 15 years and 85 years of age [24] (381 between 50 years and 69 years), albeit a population without known risk factors. If we assume a hypothetical referral group with an even distribution of subject ages from 55 years to 70 years and the same spread and trend in BMD results as the Swedish reference group, the expected mean referral rate at the non-dominant heel would be 36.7%. Adjusting for the distribution of ages seen in our 140 subjects, the figure would be 36.8%.

Discussion

The Calscan proved reliable, precise, accurate and easy to use. Calscan performance was stable within a normal range of room temperatures, and was not affected by recent movement of the device. There was no difference

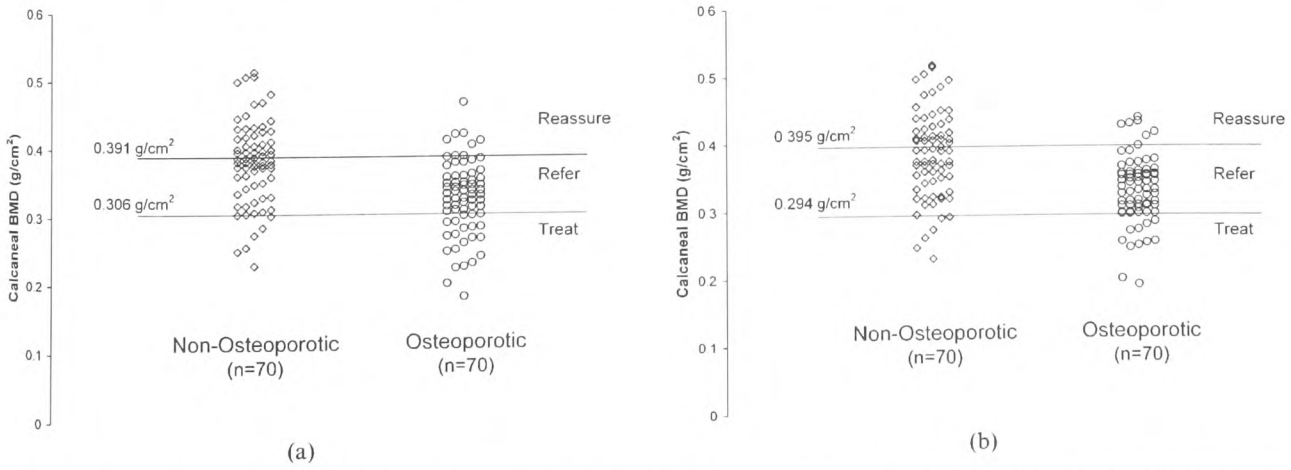

Figure 2. (a) DXL Calscan upper and lower triage thresholds for the non-dominant heel. (b) DXL Calscan upper and lower triage thresholds for the dominant heel.

Table 4. "Evaluation and Diagnostic Thresholds of the DXL Calscan". Referral by number of subjects

		Non-dominant heel	Dominant heel
Thresholds:	Upper	0.391 (−1.4)	0.395 (−1.4)
	Lower	0.306 (−2.7)	0.294 (−2.9)
Units: BMD (T-score). BMD in g cm^{-2}. T-score in standard deviations			
Above upper threshold: reassure	Non-osteoporotic	30	31
	Osteoporotic	8	7
Between thresholds: refer	Non-osteoporotic	33	32
	Osteoporotic	41	50
Below lower threshold: treat	Non-osteoporotic	7	7
	Osteoporotic	21	13
Units: number of subjects			
Referral rate		52.9%	58.6%

in performance when acquiring scans in quick succession, or with 30 min breaks between them, with the enforced 4 min period between scans appearing sufficient time for the X-ray tube to cool. Radiation dose to patient and scatter dose to operator were low and the device requires only a small controlled area. There is no lower limit of applicability and the Ionising Radiation Regulations still apply, requiring therefore the advice of a radiation protection advisor, device risk assessment, production of local rules, written procedures and appropriate training of staff.

At 1.19% CV, precision *in vivo* for our 67 precision subjects as a whole was slightly superior to the 1.24% for the Calscan and 1.28% for the GE-Lunar Pixi reported by Hakulinen et al [8], who performed repeat scans on 38 (18 male, 20 female) subjects with a mean (SD) age of 59.7 years (±9.4 years). Although at 1.30% CV the precision for our 19 osteoporotic precision subjects is poorer than the 1.09% for the 48 non-osteoporotic subjects, at 0.0042 g cm^{-2} versus 0.0048 g cm^{-2}, the mean absolute error per repeat measurement was actually lower for the osteoporotic than for the non-osteoporotic group, and so the difference in precision can be explained by the difference in the mean BMD scores for the two groups. As with all DXA systems, attainment of good precision requires technical staff to be trained, experienced and to practice good technique.

We found the coefficient of determination (R^2) with spine and total hip DXA to be 0.28 and 0.35 at the non-dominant heel. Correlation at spine was lower than the 0.59 reported by Martini et al [25], or the 0.61 reported by Hakulinen [8]. It is not clear if this is due to differences in the sample groups and the small size of the Martini and Hakulinen samples.

Using T-scores, the upper and lower triage thresholds as defined by the NOS method for the Calscan were at −1.4 and −2.7, respectively, for the non-dominant heel. These T-scores are only applicable to post-menopausal white women aged 55–70 years who meet the normal criteria for axial bone densitometry examination. As with all T-scores, the exact threshold values depend on the reference range. Were this to be changed, then the T-scores would need to be recalculated from the underlying BMD scores of 0.391 g cm^{-2} and 0.306 g cm^{-2}. In addition, the T-score thresholds of any peripheral devices employed in a triage role are likely to become more negative with advancing subject age [20], but the unreliability of spine DXA in subjects over 70 years of age makes the calculation of peripheral threshold values problematic for such a group, without resorting to total hip BMD alone.

There continues to be a growth in demand for bone densitometry services through increased awareness of health professionals and the public, rising healthcare costs of fragility fractures and the development and introduction of new bone protective treatments. The provision and availability of such services, however, remains patchy and inconsistent. In an area where demand on axial DXA is exceeding capacity, peripheral DXA could prove useful in a triage role to ensure best and most cost effective use of this resource. However, a comprehensive analysis of the resource implications of such an approach is required. Applying the triage thresholds to the population used for this evaluation would suggest that over 50% would require referral for axial DXA. As indicated, the study was not powered to provide an accurate assessment of referral proportion and the true figure is probably below 40%. Provided the cost per case for the heel DXA measurement is less than 60% that of a spine and hip measurement, there should be a net saving. Where the peripheral device is community or primary care based, there may be an increase overall in patients identified due to the more accessible nature of the service which would reduce the potential cost savings and also increase the burden on the prescribing budget.

Where there is no access to axial DXA locally, peripheral DXA may play a role in identifying those at risk of fragility fracture provided it is used with care and in appropriate populations with clearly identified clinical risk factors. The Calscan device appears suitable for either role using the thresholds derived in this study. There is a high proportion (95%) of the more metabolically active trabecular bone in the calcaneus [15] which would suggest that this site is sensitive to mechanisms affecting bone metabolism. This, together with the advantage of being a weight bearing bone, should better reflect the changes occurring at the spine and hip than at other peripheral sites. The moderate correlation between the heel and axial sites observed in this study may be due to sample bias as the subjects were drawn from those attending for bone densitometry. The lack of agreement observed generally between sites is also partly due to the varying trabecular to cortical ratios with the spine being 50% trabecular and hip 40%.

There is no published evidence to date that patients commenced on treatment on the basis of falling below the lower triage threshold by pDXA could be monitored

by pDXA. Ringe et al demonstrated promising results in heel BMD with ibandronate [26], but they employed a non-standard technique and do not compare the observed 15% increase at 2 years with the least significant change. It is also known that some bone protective treatments are only effective in reducing fractures in those defined osteoporotic by hip BMD [27]. There are no data yet on effectiveness of treatments in those targeted by the pDXA triage technique although use of the derived lower pDXA threshold provides 90% confidence that the patient would be found osteoporotic by spine and hip, with almost all the remainder severely osteopenic by spine or hip.

Use of peripheral devices in a triage role as an adjunct to an established axial DXA service could bring substantial benefits to both patient and healthcare providers, and the Calscan is well suited for this purpose. However, it should be operated only by qualified personnel, used in selected populations and results interpreted in conjunction with clinical risk factors for fragility fracture.

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The Alara Metriscan phalangeal densitometer: evaluation and triage thresholds

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ABSTRACT. The Metriscan (Alara Inc, CA) is a compact digital radiographic absorptiometry device capable of determining phalangeal bone mineral density in arbitrary units (BMD_{au}) from the second phalanges of the middle three digits. We have examined the utility and the *in vitro* and *in vivo* performances of the Metriscan, and established triage thresholds based on the UK's National Osteoporosis Society guidelines on peripheral densitometry. 170 white female participants (70 osteoporotic and 100 non-osteoporotic at the hip or spine) aged between 55 years and 70 years were recruited from patients attending for routine dual X-ray absorptiometry (DXA) examination. All participants underwent two scans of the non-dominant hand (with repositioning) and one of the dominant hand. An additional 10 participants were excluded owing to finger or hand deformities. Radiation exposure to the patient per scan was <0.1 μSv, and a controlled area of 1 m was established around the device. Phantom-based *in vitro* short-term precision (%CV) was 0.17% without, and 0.22% with, repositioning. Long-term *in vitro* precision was 0.31% over a 6-month period. *In vivo* short-term precision was 1.42% for the group as a whole, and 1.30% and 2.23% for the non-osteoporotic and osteoporotic groups, respectively. Triage thresholds for reassurance/referral or referral/treatment were 54.30 BMD_{au} and 46.89 BMD_{au}, respectively, for the non-dominant hand, and 55.02 BMD_{au} and 48.73 BMD_{au} for the dominant hand. The dominant side proved superior for triage purposes, with a triage referral rate of 44%, compared with 48% for the non-dominant hand. The Metriscan is suitable for use on post-menopausal women in a community-based setting preferably in a triage role as an adjunct to axial BMD.

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Bone mineral density (BMD) assessment plays an important role in the evaluation of patients with potential osteoporosis [1] and is typically performed by dual X-ray absorptiometry (DXA). BMD of the hip is the best predictor of hip fracture risk [2], whereas spinal BMD is most suitable for treatment monitoring [3].

Although the hip and spine are therefore the preferred sites for BMD measurement, imaging at these sites requires an axial DXA densitometer. As an alternative, there are a variety of devices available for assessing sites in the peripheral skeleton, such as the hand, forearm or heel [4]. These peripheral devices are typically smaller and cheaper, but correlation with axial hip or spine BMD varies among devices and among skeletal assessment sites. As such, peripheral assessment alone is not typically considered appropriate for the diagnosis or treatment monitoring of osteoporosis [4–8]. However, in the absence of axial DXA, current guidelines recommend that peripheral measurements can be used to aid treatment decisions in those with clearly identified clinical risk factors [5, 6, 9].

The UK National Osteoporosis Society (NOS) has proposed that peripheral devices be adopted in a triage role [9], and Blake et al [4] have defined a method by which devices can be evaluated for this purpose. For this paper, we have assessed the *in vitro* and *in vivo* performance of the Alara Metriscan (Alara Incorporated, Hayward, CA) and calculated triage thresholds using the Blake method.

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Methods and materials

The Alara Metriscan

The Metriscan is a compact digital radiographic absorptiometry device capable of measuring bone mineral content of the second phalanges of the middle three digits. The device is small enough to fit on a desktop (41 cm wide, 42 cm high, 45 cm deep) and is light enough to be transportable (<19 kg).

For an exposure, the patient removes any jewellery (when possible) from the non-dominant hand, and places the hand on the moulded support plate. Hand placement is checked to ensure the fingers are flat but not pressed down hard, and that the second phalanges of the middle three digits are within the region of interest marked on the plate.

The operator is able to take the exposure using either a button on the front of the device or a remote button

nnected by a 2 m lead. When activated, a cone beam X-y image (tube voltage, 60 kV; current, 0.333 mA) of the gion of interest is projected onto a curved storage iosphor plate mounted on a rotating drum. The drum rotated and scanned by a laser in order to excite iotons from the surface of the exposed phosphor plate, ith a photosensitive detector converting these photons an electronic signal pulse proportional to the number incident photons. A second light source then erases e plate ready for the next acquisition.

An aluminium step wedge of known thickness built to the device within the region of interest provides the libration for each image. The geometric distortion herent to projecting the image onto a drum is corrected r software before the final digital image is displayed on i LCD screen. Bone mass estimates are determined rough comparison with the step wedge, and T- and Z-ores (*i.e.* the number of standard deviations from rmal young or age-matched individuals, respectively) e derived from reference data. Results are expressed as MD but, because there is no comparison against a own bone standard, the BMD score given is an bitrary unit (BMD_{au}), rather than the usual g cm^{-2}. If quired, individual phalanges can be excluded from the alysis by the operator. There is no electronic storage of e image, but bone mass estimates and derived T- and scores can be exported to a PC via a serial cable.

vitro *methodology*

The device was operated according to the manufac-rer's instructions. Radiation protection was assessed r the local radiation protection advisor and exposure tes for both the patient and the operator were lculated. *In vitro* precision was assessed using a hand antom provided with the device. Long-term precision as calculated from 6 months' combined phantom data, ith the phantom being scanned every working day. ort-term precision was calculated from 30 phantom ans performed on the same day with repositioning, d a further 30 without.

vivo *methodology*

170 white female participants aged between 55 years d 70 years were recruited from patients undergoing utine DXA examination of the lumbar spine and hip. dial DXA scans were acquired using a GE-Lunar odigy scanner (GE-Lunar, Madison, WI). DXA of the ght hip was performed unless contraindicated. The al referral criteria for routine axial densitometry are nsistent with those of the Royal College of Physicians (UK) [10], and all participants met at least one of these criteria. The study was approved by the local research ethics committee, and informed consent was obtained from all participants.

For 12 participants, individual lumbar vertebrae showed clear signs of degenerative changes on DXA. These individual vertebrae were excluded from the DXA lumbar spine analysis. For the purposes of this study, if the lower of either L2–L4 spine or total hip BMD T-score values were below −2.5, the subject was classified as osteoporotic; otherwise, they were classed as non-osteoporotic.

Participants underwent three scans on the Metriscan — one of the dominant hand and two of the non-dominant hand. Scans were acquired in accordance with the operator manual. Where possible, rings and other jewellery were removed from the hands of the participants. Several participants were unwilling or unable to remove wedding or engagement rings but, in such cases, it was usually possible to acquire the image after pushing the rings to the proximal end of the finger.

In addition to the 170 recruits, there were a further 10 participants who were excluded owing to the Metriscan proving unsuitable for scanning. Of these, five were participants with serious rheumatoid arthritis who were unable to place their hands flat. Two participants with milder rheumatoid disease were able to place their hands flat, but had multiple rings that could not be removed owing to increased joint diameter; neither could the rings be moved proximally to such an extent as to keep them out of the image. Three further participants were excluded: one who had fused middle and index fingers; one with joint misalignment of the middle fingers; and one with no second phalanges on the index fingers.

Results

Device performance

The device was simple to operate following minimal instruction. Although the actual exposure time was less than 1 s, there was an additional 45 s processing time required for the phosphor plate to be read and the image processed.

Radiation exposure to the patient per scan was <0.1 μSv within the image field. Maximum scatter dose at 22 cm from the beam central axis was 0.2 μGy, giving a dose at 1 m of no more than 0.01 μGy. Assuming a single operator and a high patient throughput of 10 000 scans per year (~40 per day), total operator exposure would still be less than 0.1 mSv per year, and well below the recommended dose constraint of 0.3 mSv for

ble 1. Mean (±standard deviation) participant demographic variables

	Whole group		Osteoporotic		Non-osteoporotic	
	170		70		100	
e (years)	62.2	(±4.3)	62.8	(±4.5)	61.9	(±4.2)
ght (cm)	159.3	(±6.1)	158.9	(±6.6)	159.6	(±5.7)
ight (kg)	65.1	(±12.0)	62.3	(±11.4)	67.1	(±12.1)
I ($kg\ m^{-2}$)	25.7	(±4.4)	24.6	(±3.9)	26.4	(±4.6)

I, body mass index.

Table 2. Mean (±standard deviation) axial dual X-ray absorptiometry and phalangeal bone density and T-score results

		Whole group		Osteoporotic		Non-osteoporotic	
Spine L2–L4	BMD	0.969	(±0.180)	0.813	(±0.073)	1.08	(±0.148)
	T-score	−1.9	(±1.5)	−3.2	(±0.6)	−1.0	(±1.2)
Total hip	BMD	0.848	(±0.126)	0.765	(±0.086)	0.907	(±0.116)
	T-score	−1.3	(±1.1)	−2.0	(±0.7)	−0.8	(±1.0)
Dominant hand	BMD	52.79	(±6.07)	49.2	(±4.67)	55.30	(±5.68)
	T-score[a]	−0.99	(±1.46)	−1.85	(±1.12)	−0.38	(±1.36)
Non-dominant hand	BMD	51.45	(±6.11)	48.01	(±4.77)	53.86	(±5.79)
	T-score	−1.31	(±1.47)	−2.14	(±1.15)	−0.73	(±1.39)
Precision	%CV	1.42%		2.23%		1.30%	

Bone mineral density (BMD) values are given in g cm^{-2} for the spine and hip, and in arbitrary units for the hands. T-scores are given in standard deviations.
[a]Derived from the non-dominant reference range.

members of the public. A controlled area of 1 m was established around the device and it was recommended that the operator remain outside this area by using the remote cable to take exposures. The radiation protection advisor recommended that direct personal dose monitoring was not required for such low levels of anticipated dose.

In vitro *results*

The phantom provided had a nominal BMD of 58.0 BMD_{au}, corresponding to a T-score of 0.26. The average measured phantom BMD_{au} was 57.8 and the long-term precision coefficient of variation was 0.31%, based on daily scans over a 6-month period. Short-term precision was 0.17% without repositioning, and 0.22% with repositioning, for the phantom as a whole. Taking each digit of the phantom separately, short-term precision was 0.22% and 0.30% without and with repositioning for digit one, 0.32% and 0.28% for digit two, and 0.27% and 0.36% for digit three, respectively.

In vivo *results*

Subject demographic variables are summarized in Table 1. 70 participants were classified as osteoporotic by either the L2–L4 spine or total hip, whereas 100 were classified as non-osteoporotic. Metriscan and axial DXA results are summarized in Table 2; correlation between axial DXA and Metriscan results are shown in Table 3. Metriscan BMD_{au} of the dominant hand was higher than that of the non-dominant hand for the whole group, but not significantly so (p=0.052). *In vivo* precision for the non-dominant hand was 1.30%CV for the non-osteoporotic participants, 2.23%CV for the osteoporotic patients and 1.42%CV for the group as a whole. For individual digits, the precision was 2.64%CV, 1.91%CV and 2.26%CV for the three imaged digits of the osteoporotic group, and 1.75%CV, 1.51%CV and 1.88%CV for the non-osteoporotic group.

Establishing triage thresholds

In the revised NOS guidelines on peripheral DXA [4, 9], Blake et al [4] suggest the use of peripheral devices in a triage role as an adjunct to axial DXA. In doing so, they suggested a method for defining the two triage thresholds required, which can be applied to any peripheral device; indeed, this method has already been applied to several devices [9, 11]. In the Blake method, the upper of the two thresholds is set at a point above which only 10% of osteoporotic participants would fall, whereas the lower threshold is at a point below which only 10% of non-osteoporotic participants would fall. Participants who fall above the upper threshold would be assumed non-osteoporotic, whereas participants who fall below the lower threshold would be assumed osteoporotic. Participants falling between the two thresholds would be recommended for referral for axial DXA. By definition of how the thresholds are set, this method achieves a sensitivity and specificity of 90% for osteoporosis diagnosis, assuming axial DXA to be the gold standard.

For the Metriscan scanner, the upper and lower thresholds for the non-dominant and dominant hands are shown in Figure 1a and 1b, respectively. The numbers of participants falling into each triage group, and the proportion falling into the referral group and therefore requiring axial DXA, are shown in Table 4.

Of the 10 non-osteoporotic participants misclassified by Metriscan as osteoporotic of the dominant hand, 8 had severe axial osteopenia (L2–L4 or total hip T-score <−2) whereas, of the 10 non-osteoporotic participants misclassified by Metriscan as osteoporotic of the non-dominant hand, only 1 subject had severe axial osteopenia (L2–L4 or total hip T-score <−2).

Discussion

The Metriscan was compact, easy to use and took less than a minute to complete an examination. *In vivo* and *in vitro* precision values were good, and the performance was stable over the 6 months during which this study was conducted. The inability to save images electronically may have implications for centres that require images to be retained for quality assurance purposes.

In the UK, the Ionising Radiation Regulations [12] apply to any device that produces ionizing radiation, regardless of the exposure dose. Therefore, (i) the advice of a radiation protection advisor, (ii) device risk assessment, (iii) production of local rules and written procedures and (iv) appropriate training of staff are still a

e 3. Axial dual X-ray absorptiometry and phalangeal bone density correlation (Pearson's correlation coefficient)

	Spine L2–L4	Total hip	Dominant hand	Non-dominant hand
e L2–L4	1	0.664	0.562	0.539
l hip		1	0.559	0.313
inant hand			1	0.949
dominant hand				1

e 4. Breakdown of referral group by the number of icipants

	Non-dominant hand		Dominant hand	
sholds	BMD	T-score[a]	BMD	T-score
er	54.30	(−0.62)	55.02	(−0.45)
er	46.89	(−2.40)	48.73	(−1.96)
ve upper threshold: reassure				
on-osteoporotic	41		51	
steoporotic	7		7	
veen thresholds: refer				
lon-osteoporotic	49		39	
steoporotic	33		36	
w lower threshold: treat				
lon-osteoporotic	10		10	
steoporotic	30		27	
rral rate	48.0%		44.0%	

e mineral density (BMD) in given in arbitrary units. T-ore values are given in standard deviations.
rived from the non-dominant reference range.

uirement for the Metriscan. That said, the radiation e to patients and the scatter dose to operators were ; the device required only a small controlled area; l operators did not need to be individually monitored. ras possible to acquire an image using either a button the device or a cable remote. As radiation dose to the rator should always be kept to a minimum, the cable ıote — extended to 1 m — should always be used to e an exposure.

he Metriscan proved unsuitable for use on 10 out of participants; however, many participants were uited from joint rheumatoid/osteoporosis clinics, l thus the 7 participants who were excluded owing heumatoid disease may represent a higher proportion n would be found in a purely osteoporosis clinic. It y have been possible to include some of these ticipants by using the inbuilt Metriscan software to lude individual symptomatic digits, but this would d to reduced precision and possibly lower correlation h hip and spinal BMD. Hence, the Metriscan cannot recommended for use on patients with phalangeal t deformity.

ı addition, some of the patients may have been vious or current users of corticosteroids or bone tective therapy, which are suspected to have differ-al effects on cortical *vs* trabecular bone [13, 14]. As n, this may affect the relationship between axial and pheral bone density in those patients, and hence the ved triage thresholds.

he average BMD of the dominant hand was higher that of the non-dominant hand, just as calcaneal BMD is higher at the dominant heel [11]. However, the dominant hand provided a better correlation with both spinal and hip BMD than the non-dominant hand, possibly owing to wider variation between non-dominant and dominant hand activity between participants. Conversely, the calcaneus shows a higher correlation for the non-dominant heel [11] but, because both heels are load bearing, there is likely to be little variation in activity between dominant and non-dominant sides. As correlation with axial DXA is better using the dominant hand, this would seem more representative of general bone health.

At 0.559 and 0.562, the Pearson correlation coefficients between Metriscan phalangeal BMD at the dominant hand and total hip and spinal BMD values are comparable to those reported with the Demetech Calscan device (0.596 for total hip, and 0.530 for spinal L2–L4) [11], but slightly inferior to other peripheral devices, notably the Lunar Pixi (0.652 for total hip and 0.657 for spinal L2–L4) [15] and Schick Accu-DXA (0.602 for femoral neck and 0.609 for spinal L2–L4) [16]. As with other peripheral devices, there is currently no published evidence on the suitability of phalangeal assessment for treatment monitoring. The compact size, ease of use and patient acceptability of the Metriscan, however, make it well suited for use in a triage role in places where time or space are at a premium, such as GP surgeries or hospital fracture clinics.

From our population, using the dominant hand for triage referral and the Blake method, 44% of participants would have required referral for axial DXA, whereas 48% would have required referral if the non-dominant hand had been used, with an error margin of +9% owing to the small sample size. Therefore, when employing the Metriscan in a triage role, it might be better to triage by the dominant hand, as the size of the referral group is determined by the correlation of the peripheral site to hip/spinal BMD [4].

Even though the dominant hand is more suitable than the non-dominant hand for triage purposes, the non-dominant hand should still be used for direct assessment of fracture risk, as the supplied reference range data are applicable only to the non-dominant hand. Furthermore, as the triage thresholds are derived from women under investigation for post-menopausal osteoporosis, they are not applicable to men, children or pre-menopausal women.

As with all peripheral devices, employing the Metriscan in a triage role could bring substantial benefits to both the patient and the healthcare provider, assuming that the device is operated by qualified personnel and is used only on an appropriate population with clinical risk factors for fragility fracture. In such a role, the Metriscan device could reduce the number of referrals for axial DXA by ~56%.

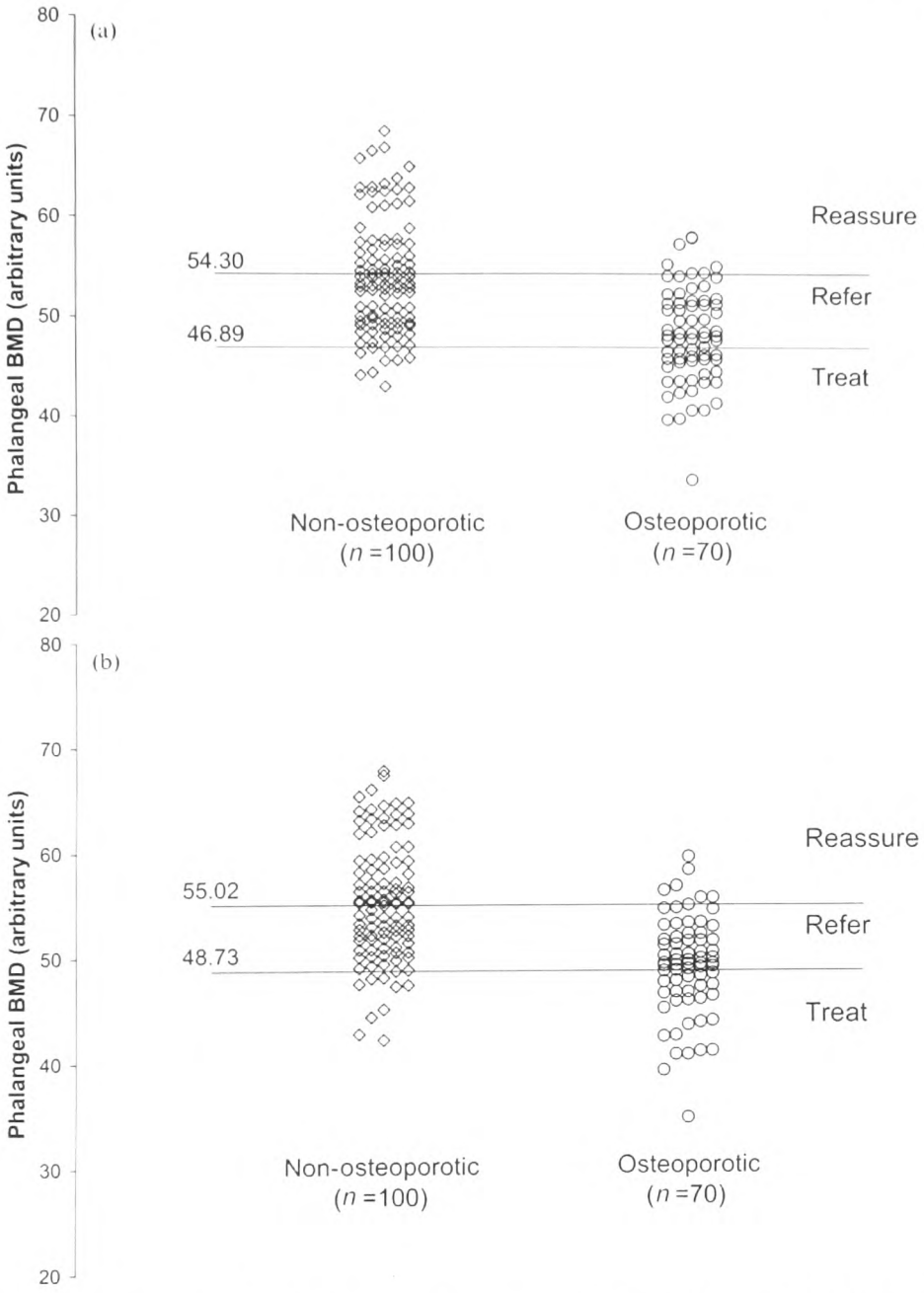

Figure 1. (a) Alara Metriscan upper and lower triage thresholds for non-dominant phalanges. (b) Alara Metriscan upper and lower triage thresholds for dominant phalanges. BMD, bone mineral density.

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APPENDIX IV

Clinical application

(Papers 8 to 12)

Osteoporosis Int (1996) Suppl. 3:S31–S36

Osteoporosis
International

The Technical and Logistical Feasibility of Population Densitometry Using DXA and Directed HRT Intervention: A 2-Year Prospective Study

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Introduction

The concept of the primary prevention of disease by screening-directed intervention is as attractive in principle as it is difficult in practice. In order for any screening programme to be acceptable, many criteria need to be satisfied [1], and these broadly reduce to three: there shall be a suitable disease, there shall be a valid test, and there shall be an acceptable intervention. If an inquiry as to the availability of any one of these three central requirements produces a negative response, then any screening exercise must be seriously flawed.

Osteoporosis is a prevalent disease in western European and North American populations and is associated with significant morbidity, particularly among postmenopausal women. It is characterized by low bone mass, microarchitectural derangement of bone tissue and a consequent increase in bone fragility and risk of fracture [2]. Quantitatively, the World Health Organization (WHO) has defined osteoporosis as being present when a site-specific bone mineral density (BMD) is shown to be more than 2.5 standard deviations (SD) below the mean of the young adult population [2].

In the United Kingdom the burden of the disease is substantial, with an estimated 60 000 fractures of femoral neck in England per year, together with 50 000 distal forearm fractures and 40 000 vertebral fractures which come to clinical attention [3]. The implication for National Health Service expenditure is also substantial, with an estimated £742m being utilized to deal with the acute care and aftercare of osteoporosis-related fractures. In the United States, Cummings et al. [4] have estimated that white women have a 15% lifetime risk of hip fracture and of Colles' fracture, while in Europe Jensen et al. [5] showed a 21% prevalence of vertebral fracture among 70-year-old Danish women. The trend in fracture incidence is also disquieting. Epidemiological data indicate that the increasing incidence of fractured neck of femur is only partially accounted for by the increased longevity of the population [6]. In other words, there may be a trend towards lower bone mass or density among elderly persons which, in conjunction with increased longevity, will place a severe strain on health resources in the next century. It should be emphasized that the disease is not only morbid but may be mortal. Within 6 months of a femoral neck fracture, patients exhibit a mortality which is 20% in excess of that expected for the age-specific control population [4].

The natural history of osteoporosis presents a *prima facie* case for examining the potential of primary prevention by screening. The disease has a relatively long "lead time" which may be taken to commence about the end of the fifth decade when BMD values begin to fall. Whether or not an individual becomes osteopenic (T-score 1–2.5 SD below the young normal mean) or osteoporotic (T-score >2.5 SD below the young normal mean) broadly depends on her individual peak bone mass, rate of postmenopausal loss and longevity. Thus there is a relatively broad window of opportunity during which a valid test might be applied to detect that sector of the general population who could be deemed to be at risk of osteoporosis.

The validity of such testing using bone densitometry has been the subject of considerable debate. It has been argued by some [7] that the clear overlap in BMD values between hip fracture patients and age-matched controls precludes the use of densitometry in assigning risk. However, BMD measurements have never been used to detect fracture itself but to stratify continuing risk, and some recent prospective data support the use of densitometry for this purpose. Wasnich and colleagues [8] showed that each 1 SD reduction in BMD at the spine was associated with an odds ratio for spinal fracture of 3.6 (95% CI 1.7–7.9). More recently Cummings et al. [9] have shown prospectively that, in respect of hip fracture, a 1 SD reduction in BMD at the femoral neck is associated with an odds ratio for hip fracture of 2.6 (95% CI 1.9–3.6). To date, BMD is the best available

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ıns of predicting osteoporosis and there is now eral agreement that for a decline of 1 SD in bone ıs, the risk of fracture at that site doubles. The inique of dual-energy X-ray absorptiometry (DXA) enerally acceptable to patients and is rapid, precise l safe as detailed below. It was, therefore, in our nion a suitable test to examine for validity as part of a mary screening programme.

The third element to be considered in evaluating such rogramme is the effectiveness of the intervention. ere is little merit in predicting, however precisely, the set of a morbid condition if the patients found to be at k cannot, or will not, comply with the preventive atment offered. The primary treatment for the pre-ntion of bone loss in the immediate postmenopause is strogen. However, several studies have shown that, en where the indication for hormone replacement erapy (HRT) is valid, the incidence of non-com-iance is substantial [10]. The principal reasons for such n-compliance usually cited are the return to cyclic eeding and a fear of breast cancer. It remains to be tablished to what extent personal awareness of an dividual's risk of osteoporosis would result in ceptance of, and compliance with, an HRT regime.

The effectiveness of oestrogen in preventing bone ss is now well attested. Epidemiological data have sociated the use of oestrogen with a 50% fall in the cidence of femoral neck fracture and those oestrogens d their delivery regimes that exert an osteoprotective ffect are known. Lindsay [11] has shown that the mmediately postmenopausal skeleton is exquisitely ensitive to oestrogen and responds by stabilizing bone rnover and eventually BMD, after producing a modest ain in density with the filling of resorption spaces.

Specifically, and in the light of the present study, Paganini-Hill et al. [12] showed that the odds ratio for emoral neck fracture in women taking oestrogen for 5 ears was 0.42. In respect of vertebral fracture a rospective study in oophorectomized women sug-ested a reduction in fracture incidence of 90% [13].

Thus it was felt that while the debate continues as to the advisability of instituting a population-based screening programme for osteoporosis, a useful contribution to that debate might be made by determining the practicality of such a measure. In the absence of the technical and logistic ability to deliver a screening programme the question of advisability becomes rather academic. Specifically, this study sought to assess the response of a perimenopausal population (aged 50–54 years) and their primary care physicians to an offer of perimenopausal densitometry. It also sought to examine the response to and compliance with the offer of an osteoprotective HRT regime over a follow-up period of 2 years, and to examine the claims made for current DXA equipment by manufacturers that it was potentially capable of handling the high-volume patient traffic required in the performance of a population-based study.

Approval for the study was obtained from the Hull and East Riding Research Ethics Committee.

Methods

General Practice Participation

From the earliest phase of the experimental design of this project, it was clear that the collaboration of the general practitioner (GP) body would be of the utmost importance. To this end, a full list of the 62 general practices serving the city of Kingston-Upton-Hull was obtained from the Family Health Services Authority (FHSA). From this list an initial pilot group of practices reflecting the broad socio-economic spectrum of the population were selected. All were practices with a particular interest in preventive healthcare and whose data archiving was of a high order. The principals in these practices were invited to visit the densitometry laboratory and take part in a seminar covering the aims and experimental design of the project. Their observations and comments on the draft communication procedures were solicited and incorporated into the final design plan. The FHSA supplied a list of all women aged 50–54 years in practices agreeing to participate. This list was then sent to the practice for verification and a final collated master list was drawn up. The exclusions applied to this list included: the presence of terminal illness, an inability to lie supine for 15 min, or a weight in excess of the densitometry couch limit of 125 kg. Patients were then invited by individual letter to attend densitometry laboratory for a measurement of hip and spine BMD. The invitation, written in standard English, included a description of osteoporosis and the nature and design of the research project. The wording of this information was discussed, amended and agreed with both GP principals and individual patients. Together with each letter, the patient received a proposed date and time for attendance at the laboratory which allowed for the patient to modify the date and time by a dedicated telephone line if the proposed time was inconvenient or she did not wish to attend.

As the study progressed general practices in groups of five or six were progressively brought into the study. Their participation began with an invitation for the partners, the practice manager and other members of the primary care team who would be in contact with screened patients, to come to the laboratory and see at first hand the technique of bone mineral densitometry and the preparation of results information. At each of these visits a full seminar was conducted which described the nature of osteoporosis, the experimental design of the study and the precise implications for the practice in the event of participation. The latter involved the communications which would be sent from the laboratory to the practice and the history and clinical examination of patients which would have to precede the prescription, if indicated, of HRT.

During the recruitment phase a high profile for osteoporosis and the screening project was maintained by the use of local radio stations, the local daily newspaper and by invited talks to interested women's groups.

A series of seminars approved for the postgraduate educational allowance was inserted into the Continuing Medical Education programme of the local Postgraduate Education Centre. These meetings proved invaluable and covered the clinical areas of menopause, the pathophysiology of bone loss and the management of HRT and other osteoprotective regimes in the primary care sector.

Laboratory and Densitometric Procedures

On attendance at the laboratory the women were asked to complete a questionnaire which sought details of medical and social factors thought to influence BMD. These data and their relationship to BMD in this cohort will be the subject of a separate communication. In particular, details were sought of age at menarche, age at menopause, occurrence of medical conditions known to affect bone and mineral metabolism, and fractures. Additionally a history was taken of hysterectomy or oophorectomy and of exposure to any agent known to affect bone mineral metabolism. Lifestyle factors including a history of dietary calcium intake and physical exercise were also sought. The questionnaires were initially administered to the patients for self completion and the completed questionnaires were then checked and reviewed by a member of the research staff.

Densitometry

The BMD of the lumbar spine (L2–4) and of the femoral neck were measured in each individual. The technique used was that of DXA and the systems used were two Lunar DPX systems (Lunar, Madison, WI) located at the Princess Royal Hospital, Kingston-Upon-Hull.

Normal Values

At the outset of the study, in 1990, the normal BMD ranges for the 50- to 54-year-old population of the United Kingdom were unknown. An early objective of the study, therefore, was to establish the normal range through patients who exhibited no clinical abnormality or medical history likely to influence bone mineral metabolism. As the study advanced and as patients numbers accumulated, those patients exhibiting clinical and historical normality were progressively incorporated into a group eventually numbering 1022 from which identification of the centile ranges was obtained.

Normative data were also established for young adults using 250 women aged 20–25 years. These data were used to derive *T*-scores (number of standard deviations from the young normal mean) for the local population as subsequently initiated by the WHO [2] for the definition of osteopenia and osteoporosis.

Women attending for osteoporosis screening whose spine or femoral neck BMD was in the lowest quartile compared with the local age-matched normal range were deemed to be at risk of developing osteoporosis. The choice of the 25th centile as the intervention level was to a degree empirical but was influenced by the stochastic mathematical model of Horsman and Burchinall [14] which predicted *inter alia* that some 66% of femoral neck fracture would occur in individuals whose BMD at age 50 years had been in the lowest quartile. Report letters were generated using locally developed computer software and sent to the GPs with recommendations regarding HRT where appropriate. The patients were instructed to contact their GP within 2 weeks for the results of their BMD measurement and to discuss any preventive treatment that may be required. The final decision on prescription of HRT was left to the GP who was, however, requested to choose a regime known to be osteoprotective. This entailed the use of 2 mg oestradiol orally *or* 0.625 mg of conjugated equine oestrogen orally *or* the 50 μg transdermal patch. Standard progestogen regimes were used in all non-hysterectomized women.

Quality Assurance of Densitometry

A rigorous quality assurance programme was initiated. This involved the daily quality assurance procedure recommended by Lunar to test the voltage setting, mechanical movements of the scan arm and X-ray source and the deviation of area and density measurements performed on a quality assurance standard containing blocks of tissue-equivalent and bone-equivalent materials of known mineral content. This procedure calibrates the machines for bone mineral content (BMC) and BMD against the standard.

The long-term precision of the densitometers was monitored by daily scanning of an aluminium phantom supplied by Lunar. This phantom consists of four segments of different sizes and thicknesses simulating the lumbar vertebrae L1 to L4 with two smaller end segments representing T12 and L5. Such a phantom was supplied with both densitometers, one with a nominal BMD for L2–4 of 1.283 g/cm^2 and the other of 1.583 g/cm^2. Both were scanned on each machine daily.

Results

Lunar DXA Performance

The densitometers proved robust, coping satisfactorily with a load of up to 12 patients per working day plus phantom scanning. Down-time as a result of mechanical or software malfunction was minimal, which was in part due to their operation of the machines within a medical physics environment where specialist engineering and computing personnel were at hand. Long-term precision (as percentage coefficient of variation) based on daily measurements of the aluminium spine phantoms, was about 0.7%. Measurement of the same phantom on

two machines demonstrated a difference between n of about 0.7%.

and Public Response

the 62 practices invited to participate one refused. A l of 7965 women aged 50–54 years were invited to nd for densitometric examination, of whom 6282 nded – a crude acceptance rate of 79%. Repeat itations to non-attenders were not issued. A random ple of 55 non-attendees was contacted and invited to te their reason. Of these, 47 (85.5%) gave reasons for n-attendance and 8 proved to have changed address. justing for a global address error as indicated by the ple, the corrected response rate for the overall study s 82.9%.

rmative and Population Data

rmative data were established using the Lunar DPX the Princess Royal Hospital. The age-matched data re based on a sample of 1022 women attending for eening and excluding those with previous medical nditions or drug treatments known to affect bone and neral metabolism. The 25th centile value for lumbar ine BMD was 1.035 g/cm^2 (T-score 1.31) and for moral neck 0.840 g/cm^2 (T-score 1.37) (Table 1). The ean (SD) age, height, weight and body mass index MI) of the 6282 patients examined were recorded. milarly, after correcting for inter-machine variation, e mean BMD (SD) of this cohort was found to be 143 (0.179) at the spine and 0.920 (0.134) at the moral neck (Table 2).

able 1. Local normative data

te	n	Age (years)	Mean (SD) BMD (g/cm^2)	25th centile	Z-score	T-score
2-4	230	20–23	1.19 (0.13)	1.110		
emoral neck	230	20–23	1.02 (0.11)	0.947		
2-4	1022	50–54	1.16 (0.17)	1.035	−0.69	−1.31
emoral neck	1022	50–54	0.93 (0.13)	0.840	−0.73	−1.37

Table 2. Local population values for women aged 50–54 years

	Mean	SD
Age (years)	52.3	1.5
Height (cm)	161.1	6.6
Weight (kg)	67.2	12.2
BMI (kg/m^2)	25.9	4.6
BMD L2–4 (g/cm^2)	1.143	0.179
BMD femoral neck (g/cm^2)	0.920	0.134

Proportions at Risk

Utilising the 25th centile values described previously, 2282 (36%) women were deemed to be at risk of developing osteoporosis (11% at the spine only, 10% at the femoral neck only and 15% at both sites). The linear correlation coefficient between spine and femoral neck BMD was 0.64 (95% CI 0.63–0.66). The relative risk of a femoral neck BMD being below 25th centile when the spine is below the 25th centile was 4.1 (95% CI 3.78–4.44).

HRT Acceptance and Compliance

Of the 1640 women "at risk" followed up at 2 years, some 215 (13%) were not offered a start or continuation of HRT therapy for the reasons shown in Table 3. Of the 1425 women who were offered a start or continuation of HRT, a total of 1127 (69%) accepted the offer. However, 298 women rejected the offer for the reasons cited

Table 3. Reasons for failure to prescribe HRT

Lost to follow-up	93 (43%)
Breast-related condition	34 (16%)
Patient deemed by GP "not at risk"	7 (3%)
Pelvis-related condition	4 (2%)
Blood-pressure-related condition	4 (2%)
Other contraindications	73 (34%)
	215

Table 4. Reasons for patient rejection of offered HRT (n=298)

Return to cycle	117 (40%)
Fear of breast cancer	34 (11%)
Fear of other side effects	56 (19%)
Acceptance of osteoporosis risk	20 (7%)
Rejection of treatment	16 (5%)
Conceptual rejection of HRT	9 (3%)
Other reasons	46 (15%)
	298

Table 5. Reasons for discontinuation of HRT

Cycle-related problems	87 (26%)
Side-effects (unspecified)	29 (9%)
Headaches	26 (8%)
Weight gain	24 (7%)
Gastrointestinal effects	15 (4%)
Depression	14 (4%)
Breast pain	8 (2%)
Fear of cancer	7 (2%)
Leg cramps	7 (2%)
Oestrogen initial effects	4 (1%)
Hypertension	4 (1%)
Developed breast cancer	2 (<1%)
Other	65 (20%)
Not recorded	43 (13%)
	335

in Table 4. At formal clinical and densitometric follow-up 2 years later, 792 women were compliant with the HRT regime, 335 women having stopped treatment for the reasons shown in Table 5. Thus, of the group of 1640 women deemed at risk and followed up, only 48% were receiving appropriate treatment 23 months later.

Discussion

In order for the procedure of densitometry to have value in the prevention of osteoporosis, and for its use to be worthy of further scientific discussion, it is essential to demonstrate three precepts, which relate to the clinical importance of the condition, the validity of the test and the acceptability of the intervention.

The condition of osteoporosis is prevalent and the clinical cost of related fracture is a burden on the public health as is the financial cost upon the public purse. The overall cost of the condition to the UK National Health Service was estimated in 1994 by the Chief Medical Officer to be £750m.

For a British woman at 50 years, the age of natural menopause, the lifetime (*c.* 30 years) risk of any osteoporosis-related fracture is 20–40% [15], the risk of femoral neck fracture being 15.6–17.5% [16]. Given the increasing longevity of our population and that mean life expectancy in England and Wales is approaching 80 years, it is unlikely that, in the absence of effective countermeasures – however applied – the overall incidence of osteoporosis-related fracture will fall. However, there are some data which suggest a slowing of the rate of increase in the incidence of osteoporosis-related fracture [17,18].

The validity of bone mass measurement as a predictor of subsequent osteoporosis-related fracture has been examined prospectively in recent studies. Cummings et al. [19] showed prospectively that a 1 SD fall in BMD was associated with a consequent doubling of the fracture risk. These data are broadly supportive of the findings of Hui et al. [20] and of Wasnich et al. [21]. The technical ability of current DXA equipment to examine a perimenopausal population has been explored in the present study. It was found that each of the two densitometers utilized was capable of examining up to 12 patients per working day, with an acceptably low down-time (resulting from maintenance or technical malfunctions) of *c.* 2 days per annum. Patient acceptability was naturally high due to the non-invasive nature of the technique and few patients were found to violate the protocol because of extreme obesity or the presence of neurological disease preventing stillness. The precision achieved was satisfactory in view of the necessity of follow-up measurements and the quality assurance programme, run daily, did not intrude significantly upon patient scanning time. We conclude that the DXA technique is potentially acceptable to patients, clinicians and health authorities as a technique for the densitometric examination of populations. Further developments should include a reduction in unit cost, reduction in scan times and provision of vertebral morphometry. However, a major weakness in the application of DXA to populations is the problem of data storage. The sheer volume of data accumulated on the processing system resulted in a serious degradation of the ability of the standard computer supplied (IBM Personal System/2 Model 70) to analyse newly added data sets in reasonable unit time. Additionally, the original floppy microdiskettes used for data archiving have had to be replaced by a higher-capacity (500 Mb) optical disk system. However, the ease with which the Lunar DPX system formulated data transfer from the machine-based PC to our statistical analysis system was a positive feature given the higher number of patients examined.

Four-fifths of the 50- to 54-year-old population complied with the invitation to attend over the life of the study. After the rate had been corrected for erroneous addresses, we therefore concluded that only about 1 in 7 of the invited population rejected the invitation to attend. Assiduous attention to written, oral and media-presented material describing the project ensured that patients were advised in clear English of the aims and objectives of the study. Clarity in language is always an asset and, we believe, has been repaid in the above compliance data.

With regard to GPs, 61 of 62 practices serving our population agreed to participate in the study. Close collaboration involving visits to the bone research and densitometry laboratory by partners, practice managers, nurses and some receptionists was found to be essential for patient management and the flow of information. The majority of GPs collaborated fully in reviewing patients 2 weeks after the scan with a view to considering HRT in those deemed at risk.

With regard to interventions, these proved to be the weakest link in the programme. Overall, of the patients who screened positive, i.e. whose BMD value placed them in the low quartile at each or both sites, only 48% had been receiving HRT continuously for 2 years since the initial examination. We have examined and presented above the reasons for non-acceptance or non-compliance by patients and for non-prescription by GPs. The principal reason for patient rejection of a GP-based offer of HRT proved to be return to cyclic bleeding and fear of breast cancer.

It was anticipated that the two principal reasons for at-risk patients discontinuing HRT would also be the return to cyclic bleeding and fear of breast cancer. However, the principal specified reasons for discontinuation of started treatment were cycle-related problems, headaches and weight gain. In respect of GPs, the initial clinical history and examination led to some 13% of patients at risk not being offered HRT. Given the age range of 50–54 years some such patients would have been premenopausal, but the principal specific reason for a non-offer of HRT was the detection by the GP of a breast-related contraindication.

The loss from treatment, for whatever reason, of over 50% of at-risk patients from a screening study is, in our

y, sufficient to invalidate the concept at the present e. Although our HRT compliance rate is substan- y higher than in other studies, it is still unacceptably . It is clear that acceptance of the concept of primary vention of osteoporosis through population bone sitometric screening will require two major ances in HRT delivery systems. First, a safe means chieving amenorrhoea on a long-term basis will have be found. Secondly, the population and its GPs will uire assurance that the risk of breast cancer during duration of the treatment, and thereafter, does not nificantly differ from that amongst a control popu- ion.

The institution of this clinical trial in Hull resulted in me 15% of perimenopausal women receiving long- m HRT for the indication of low bone mass. Given e prevalence of heart disease in UK women and the cumulating data on the efficacy of HRT in preventing rdiovascular disease [22] it is likely that the principal nefit of this bone protection programme will in fact scend upon the heart.

In conclusion, we would advocate that women at the me of menopause should be seen by their primary care hysician – not to be given HRT automatically, but to e considered for it. Where the GP or the specialist hysician or gynaecologist is persuaded that a signifi- ant health gain is attainable through its use, then, after istory and clinical examination, it should be offered to he patient. Where a significant risk of osteoporosis is uspected through past medical or past family history, lensitometry should be obtained in order to inform the lecision regarding the type and duration of the HRT egime to be offered. A direct consequence of this roject was the establishment of agreed indications for lensitometry to be funded by the local health purchas- ng authority. Only when further prospective data on the predictive value of densitometry, together with advances in HRT delivery systems, are in place will the scene be set for the final debate on population screening for osteoporosis.

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Coeliac disease and bone mineral density in adult female patients

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Abstract

A cross sectional study was undertaken to examine the relationship between coeliac disease and bone mineral density. The 135 female coeliac patients registered on the database of the Department of Gastroenterology at Hull Royal Infirmary were approached by letter, advising them of a potential risk of osteoporosis and inviting them to undergo bone densitometry. A total of 81 registered women (60%) attended the Osteoporosis Laboratory, Princess Royal Hospital and underwent dual energy x ray absorptiometry at the lumbar spine (L2–L4) and femoral neck. Historical data relating to the time of diagnosis and adherence to a gluten free diet were obtained. A control group was selected from the local normal population and was first matched for height, weight, and menopausal status. Postmenopausal patients were then further matched to controls of equivalent menopausal age. In coeliac patients, bone mineral density expressed in g/cm^2 as mean (SD) was significantly lower at the lumbar spine (1·076 (0·186)) than in the control group (1·155 (0·143), $p<0·001$). This was also the case at the femoral neck (0·887 (0·142) *versus* 0·965 (0·127), $p<0·001$). When the coeliac patients were stratified by menopausal status, it was found that femoral neck bone mineral density was significantly below control values in both premenopausal and postmenopausal women. Spinal bone mineral density exhibited a significant decrement only in the postmenopausal group. The age at diagnosis of coeliac disease and adherence to a gluten free diet did not influence bone mineral density at either hip or spine. These results confirm coeliac patients' higher risk of osteopenia. Coeliac disease should be added to the list of medical conditions which constitute an indication for bone densitometry in order that the individual risk of osteoporosis related fracture may be determined.

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Keywords: coeliac disease, bone, densitometry, osteoporosis.

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It has long been recognised that coeliac disease may be associated with disorders of the skeleton. Over 60 years ago Bennett *et al*[1] reported major skeletal deformities in patients diagnosed in adult life as having Gee's disease or idiopathic steatorrhoea and the presence of biochemical derangement of calcium metabolism was noted by Salvesen and Boe[2] in 40 out of 90 patients with adult sprue. More recently, Harris *et al*[3] comprehensively examined the bone and mineral metabolism of 118 coeliac patients utilising Ca^{47} balance studies, bone biopsy, and skeletal x ray. Some 63% of these patients had a significant disturbance of bone metabolism, the most common of which was osteomalacia with or without concomitant osteoporosis, the latter condition being rarely present alone. In a study of 22 treated adult coeliacs, Molteni *et al*[4] utilised single photon absorptiometry to measure bone mineral density (BMD) at the distal radius. These patients' BMD values did not differ from those of age matched controls. In 29 untreated adult patients, however, BMD was significantly lower than in age matched controls but did not correlate with the severity of clinical abnormalities. In an intervention study, Caraceni *et al*[5] noted that, in 20 untreated coeliac adults, BMD at the distal radius was significantly lower than in age matched controls and that biochemical parameters indicated accelerated bone turnover in the coeliac group. They further observed that 12 months after the institution of a gluten free diet no significant change in BMD had occurred: a result interpreted by these authors as indicating arrest of further bone loss. Equally, no restitution of previously lost bone mass was observed. The basic pathology underlying mineral metabolic derangements in coeliac disease has been well reviewed by Cooke and Holmes.[6] These workers reported that there is no compelling evidence for excessive excretion of calcium bound to faecal fat and that the basic anomaly is likely to be vitamin D malabsorption consequent on raised intraluminal pH. Vitamin D dependent calbindin-D9K is severely depleted in coeliac disease and may mediate calcium malabsorption in this condition.[7] Calmodulin activity, however, seems to be unchanged.[8]

Taking the opposite tack, Lindh *et al*[9] observed that of 92 patients with proved osteoporosis, 11 (12%) exhibited the presence of antigliadin IgA, a prevalence significantly in excess of that found in the general population. Interestingly, these patients displayed no anomaly of mineral metabolism or calcium malabsorption, and in only three was a histological diagnosis of coeliac disease established. Subclinical coeliac disease thus seemed to be over represented in osteoporotic men and women.

Recently, MacFarlane *et al*,[10] using dual energy x ray absorptiometry (DEXA) at hip and spine, found a decrement of BMD at both sites in 50 coeliac patients compared with age and sex matched controls. Butcher *et al*,[11] in a

study of 20 patients concurred that reduced BMD was prevalent in women with coeliac disease and that the detection of osteopenia requires densitometry. In this study, adjustment for body mass index (BMI), dietary control, or disease duration did not affect the overall difference observed between coeliac patients and healthy controls.

The above observations suggest a relationship between coeliac disease and BMD, the latter being the prime determinant of risk of osteoporosis related fracture.[12] In order to thoroughly examine this relationship we have conducted a study of BMD in coeliac patients with rigorous control for potential confounding variables including menopausal age, BMI, hysterectomy, and exposure to hormone replacement therapy.

Patients and methods

One hundred and thirty five women, aged 20–70 years, with histologically proved coeliac disease and registered with the Department of Gastroenterology at Hull Royal Infirmary were invited to attend Princess Royal Hospital for densitometric examination of the spine and hip. Eighty one patients (60%) attended. After obtaining informed consent, a clinical questionnaire was administered which enquired into the presence of factors known or suspected to influence BMD. These factors included smoking, alcohol use, amount of exercise taken, drug therapy including hormone replacement therapy (HRT) and corticosteroids, or prior hysterectomy. With regard to coeliac disease itself, the time since diagnosis and the degree of adherence to a gluten free diet were also recorded. Weight and height were measured and the BMI was expressed in standard form as weight (kg) divided by height (m^2).

BMD at the spine (L2–L4) and hip (femoral neck) were measured by DEXA. The apparatus used was the Lunar DPX (Lunar Radiation Corporation, Madison, Wisconsin, USA). Quality assurance studies have shown that in our hands the equipment has a coefficient of variation of 0·78% for spine and 1·2% for hip BMD.

A matched control was selected for each coeliac patient. The premenopausal controls were selected from 230 healthy women in the third decade, attending for BMD measurement. The postmenopausal controls were selected from our database of values obtained from 6426 women age 50 to 70. Matching was performed in respect of menopausal status, height, and weight. Postmenopausal patients were then further matched according to the time elapsed since the menopause (menopausal age). Women within 10 years post menopause were matched exactly for menopausal age, women between 10 and 25 years post menopause were matched for menopausal age ±2 years, and those over 25 years post menopause were matched for menopausal age ±6 years. Each control patient was selected to match the study patient to within ±2 cm of height and ±2 kg of weight. Five patients could not be matched with this precision and were assigned controls whose BMI were within ±2·5 of the index case.

Statistical analyses were performed using *Epi Info 5.01b* (World Health Organization, Geneva, Switzerland) and *Kwikstat 2.00* (Texasoft/Mission Technologies, Cedar Hill, Texas, USA). Two sided tests were used with the level of statistical significance set at 0·05. Parametric variables were compared using the *t* test (ANOVA and paired *t* test) and non-parametric variables were compared using the χ^2 test, or Fisher's exact test where the numbers were too small to allow accurate interpretation of the χ^2 test. Multiple regression analysis was performed to test the effect of BMI, menopausal age, adherence to diet, and duration of coeliac disease on BMD. All values are stated as mean (SD).

The research protocol was approved by the Hull and East Yorkshire Ethics and Clinical Trials Committee.

Results

Eighty one coeliac disease patients attended for measurement of bone mineral density. Fifty two were premenopausal and 29 postmenopausal. The latter had a mean (SD) age of 59·2 (8·6) years with a range of 40–77 years. There were no differences between coeliac and control groups in respect of hysterectomy, exposure to hormone replacement therapy, corticosteroids, exercise, or tobacco or alcohol consumption (Table I). Age at diagnosis of coeliac disease and institution of a gluten free diet ranged from 0 to 41 years with a median of 8 years. Fifty eight patients reported they had always adhered to a gluten free diet, 17 patients usually adhered, and six patients never adhered. Eighty one matching controls were selected from the normal databases described above. BMD was expressed using the standard area density notation of g/cm^2 presented below as means (SD).

Overall, the coeliac patients (n=81) showed a significantly lower mean (SD) spinal BMD (1·076 (0·186)) than the control group (1·155 (0·143); p<0·001). Similarly, BMD at the femoral neck in the coeliac group was 0·887 (0·142) whereas that of the control group was 0·965 (0·127); p<0·001. When the two groups were stratified according to their menopausal status, the postmenopausal coeliac patients

TABLE I *Occurrence of potential confounding variables in coeliac disease patients and control subjects*

Parameter	Group		Significance
	Coeliac	Control	
Ever smoking	44/81	49/81	NS*
Median (range) alcohol consumption (U/wk)	2 (0–21)	3 (0–21)	
Exercise (no):			
Athletic	4	3	NS**
Normal	75	78	NS**
Restricted	2	0	NS**
Ever use of:			
Corticosteroids	10/81	7/81	NS*
HRT	9/29	12/29	NS*
Prior hysterectomy	12/29	14/29	NS*

*χ^2 test; ** Fisher's exact test.

TABLE II *Bone mineral density (g/cm²) of the spine (L2–L4) and femoral neck in patients with coeliac disease and their matched normal controls. Values are mean (SD)*

	Group		
	Coeliac	*Control*	*p Value*
Overall:	(n=81)	(n=81)	
L2–L4	1·076 (0·186)	1·155 (0·143)	<0·001
Femoral neck	0·887 (0·142)	0·965 (0·127)	<0·001
Postmenopausal women:	(n=29)	(n=29)	
L2–L4	0·924 (0·14)	1·129 (0·18)	<0·001
Femoral neck	0·785 (0·10)	0·885 (0·11)	<0·001
Premenopausal women:	(n=52)	(n=52)	
L2–L4	1·160 (0·151)	1·169 (0·117)	NS
Femoral neck	0·943 (0·129)	1·010 (0·114)	<0·001

(n=29), had a significantly lower spinal BMD of 0·924 (0·14) than the control value of 1·129 (0·70); p<0·001. In this group, the femoral neck BMD of 0·785 (0·72) was also significantly below the control group value of 0·885 (0·55); p<0·001.

The premenopausal coeliac patients (n=52) did not show a significantly different spinal BMD (1·160 (0·151)) when compared with their controls (1·169 (0·117)). However, at the femoral neck, the premenopausal coeliac patients did show a significantly lower BMD (0·943 (0·129)) than their controls (1·010 (0·114); p<0·01) (Table II).

Using multiple regression analysis, neither the time since diagnosis of coeliac disease nor reported adherence to gluten free diet was found to exert any significant influence upon BMD. However, BMI was positively correlated with spinal but not femoral neck BMD. Menopausal age correlated significantly with both spinal and femoral neck BMD (Table III).

Discussion

This study confirms that coeliac disease adversely affects bone mineral density, and that the relationship holds when female coeliac patients are compared with strictly selected controls matched for sex, height and weight, menopausal status and, where applicable, menopausal age. It can be argued that the premenopausal controls should be age matched too. Published reports are divided about the impact of age as a single factor on BMD in the healthy premenopausal patient, however,[13 14] and for practical purposes it is generally agreed that peak bone density, achieved in the early third decade is essentially the value with which women later approach the climacteric.

The exact mechanism of the development of osteopenia and osteoporosis in the coeliac patient is incompletely understood.[19] There is no direct correlation between bone derangements and steatorrhoea,[15] although the institution of a gluten free diet has been reported to have a beneficial effect on BMD.[4 16] Possible but unproved mechanisms leading to osteopenia in the coeliac patient include a reduced intestinal surface area due to the characteristic villous atrophy,[17] saponification of intestinal calcium with unabsorbed fats with increased faecal calcium excretion,[6] secondary hyperparathyroidism due to reduced absorbtion of calcium,[3] and decreased absorbtion of vitamin D.[18]

TABLE III *Multiple regression analysis between body mass index (BMI), menopausal age (MEN), adherence to diet (ADH), duration of disease (DUR), and bone mineral density (BMD) of the lumbar spine and femoral neck*

BMD	*BMI*	*MEN*	*ADH*	*DUR*	r^2
L2–L4	p<0·01	p<0·001	NS	NS	0·45
Femur	NS	p<0·001	NS	NS	0·34

Present lack of understanding of the exact mechanisms involved, makes it difficult to explain our observation that coeliac disease in the premenopausal patient seems to affect the femoral neck BMD alone. This could reflect a differential impact of the calcium/vitamin D malabsorption of coeliac disease on the mainly cortical bone of the femoral neck compared with its effect on the mainly trabecular bone of the lumbar vertebrae. The latter, in the presence of adequate endogenous oestrogen, may be able to maintain BMD in the face of malabsorption of mineral. After the menopause, the loss of endogenous oestrogen removes the spinal protection and both sites then exhibit substantial decrements on BMD when compared with matched non-coeliac controls. On the other hand, this apparent difference could be artefactual, due to the different populations used for selecting the premenopausal and postmenopausal control groups. We would caution that the use of postal recruitment of a registered coeliac population may incur bias. For example, knowledge that BMD was to be measured may have encouraged attendance by a sample partially selected by a positive family history of osteoporosis or a previous history of fractures.

What advice should be offered to patients with coeliac disease to protect them against osteoporosis? Although our multiple regression analysis did not show a significant affect of dietary adherence upon BMD, the numbers of non-adherers was small and the true influence of a gluten free diet upon BMD will require to be assessed in a larger, and ideally, prospective study. But consideration should be given to performing bone mineral densitometry either at the time of diagnosis or at the time of menopause, in order to establish basal values of mineral density at the key areas of spine and hip. The premenopausal patient may then be followed up with two repeat densitometry examinations at yearly intervals in order to establish that BMD is stable. Such patients may then be discharged from densitometric follow up until menopause when a further examination will determine if her BMD requires intervention with HRT or an alternative bone-sparing regime. All postmenopausal patients with coeliac disease should undergo BMD measurement at hip and spine and should be considered for treatment with specific bone-sparing regimens, should a diagnosis of osteoporosis be established.

It should, however, be emphasised that the natural history of bone mineral density in the coeliac patient will remain obscure until prospective studies utilising precise measuring techniques such as DEXA become available.

For the moment coeliac disease should be added to the list of medical conditions whose presence constitutes an indication for bone densitometry.

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Factors affecting long-term adherence to hormone replacement therapy after screening for osteoporosis

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Key words: SCREENING FOR OSTEOPOROSIS, LONG-TERM ADHERENCE TO TREATMENT, HORMONE REPLACEMENT THERAPY

ABSTRACT

Objective To investigate factors likely to influence adherence to hormone replacement therapy (HRT) in women known to have low bone mass.

Study design This was a prospective study of bone mineral density screening in 6282 women aged 50–54 years.

Results Low bone mass at either the hip or spine was found in 1462 women. The principal route of HRT delivery, transdermal or oral, as well as the presence of climacteric symptoms before starting treatment, did not influence adherence. However, adherence to HRT type was significantly superior in hysterectomized women taking unopposed estradiol (median 32 months) compared with those on sequential HRT (median 28 months; $p = 0.011$). Overall, a 5-year adherence to HRT of 61% was achieved.

Conclusion Approximately 34% of women starting HRT are likely to stop in the first 2 years of use. Following this, the discontinuation rate is low. The combination of knowledge of risk for osteoporosis and regular follow-up positively influences long-term adherence to HRT.

INTRODUCTION

Hormone replacement therapy (HRT) is one of the treatments of choice for the prevention of bone loss, and there are recent data to confirm its long-term effectiveness in the reduction of hip fracture[1]. It confers additional benefits such as the relief of physical and psychological symptoms of the climacteric. Universal treatment of osteopenia – low bone mass – with HRT has been advocated[2], but has proved unrealistic. Such a strategy would have considerable financial and human-resource implications, and its effectiveness would be compromised by poor adherence. Climacteric symptom relief thus remains the most common reason for prescribing HRT[3]. However, among women who receive prescriptions, only 25–40% will adhere to therapy for more than 1 year and, within 3 years, 75–80% will have stopped treatment[4]. The return of cyclic or unscheduled bleeding, together with fear of breast cancer, is one of the most commonly cited reasons by patients for discontinuation[5,6]. Period-free HRT regimens may thus conceivably influence adherence, and have been reported to improve adherence in some but not all studies[7,8]. Interestingly, prior hysterectomy does not appear to affect the rate of discontinuation[4], an apparent

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challenge to the central issue of bleeding as a disincentive to adherence[6]. Transdermal regimens are more likely to be discontinued than oral ones[4].

Awareness of the risk of osteoporosis might significantly influence adherence. In one study, 96% of women interviewed said that they would consider HRT if their bone densitometry scan disclosed an increased risk of osteoporosis[3]. In another, however, only 78% of women at risk accepted HRT following densitometric screening, and of those almost 40% discontinued treatment within 8 months[9].

In this study, we have examined how an individual patient's knowledge of her risk of osteoporosis, plus regular scheduled follow-up for up to 5 years, influence acceptance and long-term adherence to HRT regimens.

METHODS

Between 1989 and 1993, 6282 women aged 50–54 years underwent femoral neck and spinal bone mineral density (BMD) assessment by dual energy X-ray absorptiometry (DXA) as part of a collaborative exercise to determine the technical and logistical feasibility of a population-based osteoporosis screening program. The study was approved by the local ethical committee. All general practitioners (GPs) were approached regarding participation in this study, and attended a presentation and discussion with the principal investigators. The GPs were instructed in the methods to be used in this study for the interpretation of bone densitometry results, and identification of patients at high risk of future fragility fracture. The benefits and risks of HRT and dietary and life-style issues affecting bone density were also presented. The GPs were instructed to see and advise those women defined as being at risk, and, where appropriate, offer HRT from a menu of bone-protective regimens. The study protocol was not prescriptive in terms of continued support and counselling of the patient by primary care, as the aim was to observe compliance under standard clinical practice.

In this large cohort of women, 2282 (36%) were found to have BMD at either the hip or spine below the 25th centile and, following the guidelines applicable at the time, were classed as being at risk of osteoporosis. According to the World Health Organization (WHO) classification, these women are all below the osteopenic threshold[10]. Entire 5-year data sets for HRT acceptance and adherence were available for only 1462 women (23%), who were hence considered in this article.

The 61 general practices collaborating in the study were provided with a menu of HRT regimens which were known, through clinical trials, to be osteoprotective. These were Prempak C®, Cycloprogynova®, Menophase®, Estrapak® and Estracombi® for non-hysterectomized women and Premarin® and Estraderm® patches for women without a uterus[11]. The practitioners were asked to recommend commencement of HRT if the patient was agreeable and clinically suitable. Similarly, if HRT had already been started, its continuation was advocated. The types of HRT preparations used at baseline are reported in Table 1. Changes in HRT regimen were allowed if, at any time, the current therapy proved to be unacceptable or intolerable.

On attendance for DXA, data were collected by questionnaire on relevant medical and social factors, presence of menopausal symptoms and HRT exposure. Patients were informed of their bone density results by their GP, who was then responsible for the initiation of treatment and for its day-to-day management. Patients were offered further densitometry assessment at 2 and 5 years. At each follow-up visit, patients were questioned on adherence to treatment.

Statistical analysis was performed using Epi Info 6 (Centers for Disease Control and Prevention, Atlanta, GA) and Statistical Package for the Social Sciences (SPSS, Chicago, IL) software. Demographic data were analyzed using an independent two-sample t test for normally distributed data and the Wilcoxon two-sample test for other comparisons. The χ^2 test was used to compare prevalence of menopausal symptoms and prior hysterectomy. Differences were considered to be statistically significant if $p < 0.05$.

Table 1 Number of women using specific hormone replacement therapy (HRT) preparations at baseline

	Established HRT users ($n = 180$)	*De novo HRT users* ($n = 838$)
Unopposed estrogen	$n = 54$	$n = 163$
Transdermal	31 (17.2%)	79 (9.4%)
Oral	22 (12.2%)	82 (9.8%)
Implants	1 (0.6%)	2 (0.2%)
Estro-progestogens	$n = 126$	$n = 675$
Oral	104 (57.8%)	509 (60.7%)
Transdermal	13 (7.2%)	39 (4.7%)
Livial®	3 (1.7%)	21 (2.5%)
Kliogest®	—	9 (1.1%)
Not specified	6 (3.3%)	97 (11.6%)

Treatment adherence analyses were conducted on an intention-to-treat basis for all eligible patients. Survival was measured from the date of first starting the treatment to date of discontinuation of that particular treatment. Patients still on the original treatment at 57 months had their treatment duration time censored at 57 months. The original recommendation to GPs was to maintain the patient on HRT for 5 years only. At the time, this was thought to be the optimal time to incur bone-protective effects with minimal increased breast cancer risk. Patients were generally commenced on their treatment 3–12 weeks following their densitometry assessment; hence, at the 5-year follow-up, *de novo* patients adherent to HRT would report treatment adherence times of 57–59 months. Survival estimates were calculated using the Kaplan–Meier method, and survival curves were compared using the log-rank test for equality.

RESULTS

Entire 5-year data sets for HRT acceptance and adherence were available for only 1462 of the 2282 women who were considered at risk of osteoporosis. Of these women, 180 (12%) were already taking HRT at the commencement of the study and continued with their regimen, while 838 (57%) of the remainder were found to be suitable for HRT and, after consultation with the practitioner, on the basis of the densitometric result were advised to start treatment *de novo*. A total of 444 (30%) women were not commenced on treatment, since 179 had a contraindication to its use and 265 (60%) rejected the offer. The 180 women who were current HRT users at entry had been on treatment for an average of 50.3 months (standard deviation (SD) 28.4 months), and, of them, 159 (88%) were still on treatment 2 years after screening, compared with only 550 (66%) of the *de novo* group. This difference was statistically significant ($\chi^2 = 36.12$; $p < 0.01$). However, after the first 2 years of use, HRT discontinuation became similar in the two groups at 11% for established HRT users and 9% for those starting HRT *de novo* (Figure 1).

The baseline anthropomorphic characteristics of women who were established or *de novo* users of HRT are presented in Table 2. There were no statistically significant differences in age, body mass index (BMI) or BMD at the hip between the two groups. However, spine BMD was, on average, 3% higher in established HRT users (1.029 g/cm^2) than in women starting *de novo* (0.997 g/cm^2) ($p = 0.004$). One hundred and fifty-seven women (87%) who were established HRT users had climacteric symptoms before starting HRT, compared with 550 (65%) *de novo* users ($p < 0.001$). Established HRT users were also more likely to have undergone hysterectomy: 62 women (34%) versus 180 (21%) women who were *de novo* starters ($p < 0.001$) (Table 2).

Information on the presence or absence of climacteric symptoms before starting HRT was available in 1012 (99%) of the 1018 women who either started HRT *de novo* or were on HRT at the time of densitometry screening. Their baseline anthropomorphic characteristics are presented in Table 3. There were no differences in age, BMI or BMD at the hip or spine between the symptomatic and asymptomatic groups. As expected, those with symptoms had a lower mean menopausal age (years of amenorrhea) than those without.

Climacteric symptoms, which are mainly vasomotor or psychological, might have influenced uptake and continuation of HRT in a total of 708 (70%) women, while 304 (30%) women were asymptomatic and thus based their decision to start or continue HRT solely on the basis of the bone density results.

At the 5-year follow-up, 445 (63%) symptomatic and 178 (58%) asymptomatic women were still taking HRT. The difference was not statistically significant ($\chi^2 = 1.66$; $p = 0.20$).

A total of 242 women (24%) in the study group had undergone hysterectomy at a mean age of 41.3 (SD 6.1) years. The adherence rate to treatment at 5 years was 66% ($n = 160$) among hysterectomized and 60% ($n = 465$) among non-hysterectomized women ($\chi^2 = 2.99$; $p = 0.08$).

For the route of administration analysis, 817 (87%) of the 945 patients with valid information discontinued their initial HRT therapy within 57 months of beginning: 700 oral and 117 transdermal (Figure 2). The median duration of time on HRT was the same for both routes of administration (oral: median 27 months, 95% confidence interval (CI) 25–28 months; transdermal: median 27 months, 95% CI 23–31 months). As expected, the log-rank test showed no statistically significant difference between the duration times (log-rank $\chi^2 = 0.27$; df = 1; $p = 0.61$).

For the type of HRT analysis, 685 (85%) of the 807 patients with valid information discontinued their initial HRT therapy within 57 months of beginning: 542 sequential and 143 unopposed (Figure 3). The median durations of time on HRT were statistically significantly different from

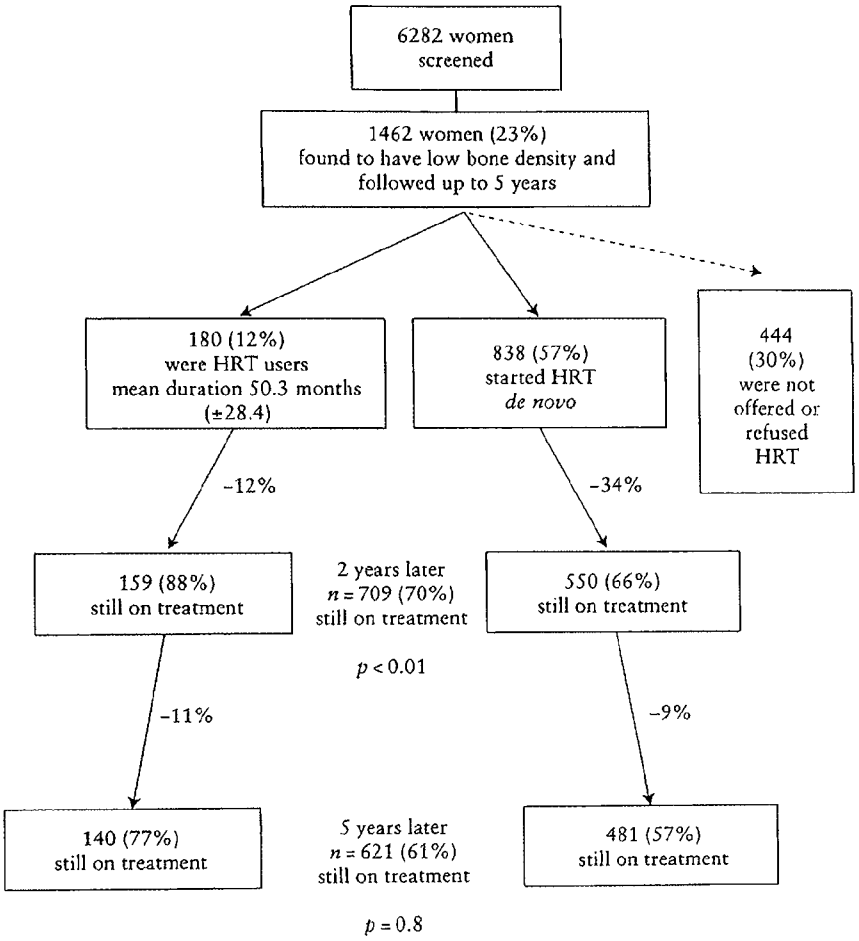

Figure 1 Natural history of hormone replacement therapy (HRT) adherence

Table 2 Baseline characteristics for those who started or continued hormone replacement therapy (HRT) on the basis of densitometry (n = 1018). Values are expressed as mean ± standard deviation, two-sample t test, or n (%), χ^2 test

	Established HRT users (n = 180)	*De novo HRT users* (n = 838)	*p Value*
Age (years)	52.5 ± 1.4	52.5 ± 1.4	0.9
Body mass index (kg/m^2)	24.6 ± 3.3	24.7 ± 3.9	0.8
Body mineral density (g/cm^2)			
spine	1.029 ± 0.108	0.997 ± 0.115	0.004
hip	0.822 ± 0.76	0.812 ± 0.82	0.16
Climacteric symptoms	157 (87)	550 (65)	< 0.001
Hysterectomy	62 (34)	180 (21)	< 0.001

each other (log-rank χ^2 = 6.45; df = 1; p = 0.011). The duration times for the two groups were, unopposed: median 32 months, 95% CI 28–35 months and sequential: median 28 months, 95% CI 26–29 months.

DISCUSSION

The described combination of risk assessment and follow-up achieved a 61.3% long-term (5 years) adherence to HRT, one of the highest adherence rates so far reported. Previous studies have

Table 3 Characteristics of patients with or without climacteric symptoms before starting hormone replacement therapy (HRT) (n = 1012). Values are expressed as mean ± standard deviation, two-sample t test

	Symptomatic (n = 708)	*Asymptomatic* (n = 304)	*p Value*
Age (years)	52.4 ± 1.4	52.6 ± 1.4	0.12
Body mass index (kg/m^2)	24.8 ± 3.9	24.4 ± 3.4	0.11
Body mineral density (g/cm^2)			
spine	1.006 ± 0.12	0.994 ± 0.12	0.12
hip	0.816 ± 0.081	0.808 ± 0.080	0.17
Years postmenopause	6.5 ± 5.2	7.4 ± 5.3	0.02

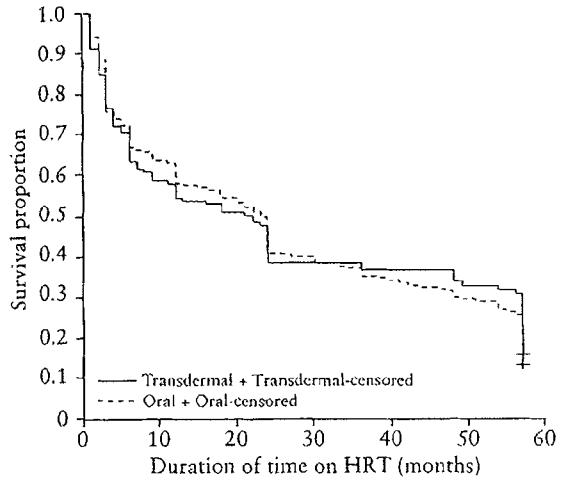

Figure 2 Kaplan–Meier estimates for treatment adherence by route of administration of hormone replacement therapy (HRT): transdermal, 22 (15.83%) censored cases; oral, 106 (13.15%) censored cases; log-rank $\chi^2 = 0.27$, $p = 0.61$

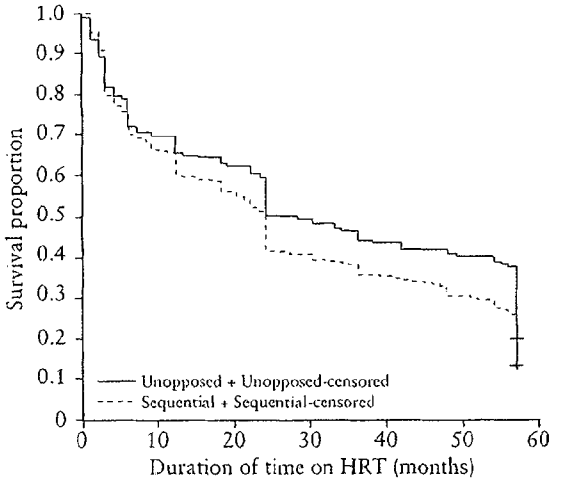

Figure 3 Kaplan–Meier estimates for treatment adherence by type of hormone replacement therapy (HRT): unopposed, 36 (20.11%) censored cases; sequential, 86 (13.69%) censored cases; log-rank $\chi^2 = 6.45$, $p = 0.011$

evaluated adherence to treatment over relatively short periods. Ravnikar[12] in a survey recorded a 30% adherence rate after 9 months of treatment, while Sullivan[13] reported that only 40% of women in the general population were still taking HRT at 1 year. One study evaluated adherence to treatment beyond 1 year, and found a poor 4-year adherence rate of 20%[14], with the best rates recorded in those individuals commenced on HRT because of clinical risk factors for osteoporosis. Knowledge of the results of bone densitometry has been shown to influence osteoporosis-preventive behavior substantially[15]. Rubin and Cummings[16] found that 94% of women who had low bone density results began at least one type of preventive measure, compared with 56% of those who had a normal result.

If knowledge of risk influences uptake, the central issue becomes that of adherence to therapy. In the Postmenopausal Estrogen/Progestin Interventions (PEPI) trial, 81–86% of participants taking either sequential or continuous HRT were continuing after 3 years[17]. In clinical trials, participants are often volunteers, whose motivation to continue study medication is generally higher than that of the normal population[18]. Choice of treatment, education and, above all, follow-up clinic visits may be important to enhance motivation and manage side-effects. Discontinuation with HRT occurs primarily in the first few years of use. In the present study, about 23% of women already established on treatment before the start discontinued before 5 years, at a rate of about 11.5% between densitometric assessments. Women who started HRT *de novo* showed the largest discontinuation rate during the first 2 years of treatment (34%), while in the subsequent 3 years, the discontinuation rate was similar in both groups at 9% in *de novo* users and 11% in established users ($p = 0.8$). This supports the findings of others that, after the initial period of adaptation, almost 80% of

women will continue treatment long term[19]. Support and regular follow-up is thus required, particularly during the first few months of starting HRT treatment when side-effects[6] are more likely to occur and cause treatment discontinuation. The main difference between the present study and others where lower adherence rates were obtained[9] was the recall system and repeated densitometry. Densitometric follow-up is not generally advocated in patients on osteoprotective treatment, but regular review, either by densitometry or by measurement of bone turnover markers, may prove important as a regular means of feedback to patients to secure adherence, and as a means of identifying non-responders. Garton and colleagues found that 96% of women would be willing to consider HRT if the bone scan suggested an enhanced risk of future osteoporotic fractures, and as many as 85% would take HRT for as long as their doctor recommended it[3]. Densitometry is thus a powerful tool to enhance motivation both to initiate and to continue treatment, particularly when this is required long term for indications such as osteoporosis prevention.

It has been suggested that treatment adherence rates over 30% would make osteoporosis screening cost-effective[20]. We have achieved continuation rates of over 60% at 5 years with HRT alone among women in their sixth decade. Adherence rates to treatment might have been even higher if women had had available, at the time, a wider choice of treatment such as bisphosphonates and a selective estrogen receptor modulator (SERM) in addition to HRT. In this study, only 48% of the overall total 1640 women found to be at risk of osteoporosis were receiving appropriate treatment after 2 years[6].

It might be argued that women who volunteer for bone density screening programs may be an intrinsically higher-risk group who are concerned about osteoporosis because of previous fractures, current risk factors or family history. They would hence be more likely to comply with treatment compared with women in the general population. However, since the offer of densitometric examination was made to a total of 7965 women aged 50–54 years of whom 6282 (79%) attended, and since the corrected acceptance rate to the offer of densitometric screening was 6282 (83%)[5], this sample should be reasonably representative of the overall population concerned. Of the 2282 women who were identified at the initial screening visit as being 'at risk', 820 (36%) were lost to follow-up; thus, 1462 (64%) are the subject of this review. We suspect that the substantial loss to follow-up is due to multiple factors, including breakdown in communication between the Centre, the patient and the GP concerned, and this will be the subject of a future article.

Patients attending at menopause clinics complain primarily of climacteric symptoms[21], and many women commence HRT for symptom relief. Our data, contrary to those of others[22], fail to show any positive influence of climacteric symptoms, present at the institution of treatment, on long-term treatment adherence.

The return of monthly bleeding is often cited as one of the main reasons for discontinuation. Sequential combined HRT regimens are associated with cyclic bleeding, while continuous combined regimens should achieve amenorrhea. We could not reliably compare adherence rates of sequential versus continuous combined regimens as the latter were only launched in the UK in 1995, some 5 years after the start of this study. Women in this trial were recruited between 1989 and 1993, and therefore the majority of them were offered, and continued with, sequential HRT. After 2 years, the difference in continuation between hysterectomized women on unopposed estrogen and those with a uterus on sequential combined regimens became more apparent (Figure 3). This is in agreement with the data of Ettinger and Pressman[4]. Contrary to what is commonly believed, regular withdrawal bleeds do not appear to affect adherence adversely at the start of treatment, but become an issue after 12–24 months of treatment. Lack of bleeding, such as that reliably achieved with hysterectomy, may thus enhance treatment adherence[23]. Route of administration might also conceivably influence treatment adherence. Transdermal HRT was found to lower adherence in one study[4], but not in another[24]. Among women in the present study, adherence at follow-up was similar for transdermal and oral administration.

In conclusion, clinical risk factors have been shown to be unreliable as a means of identifying women at high risk of osteoporosis, and the variable most strongly predictive of fracture risk is bone mineral density[25]. The case for screening all postmenopausal women by measurement of bone mineral density has been unacceptable for several reasons, one of which was that adherence to treatment following screening was unknown. Our data show that targeting treatment to women at risk, combined with regular densitometric follow-up, can achieve high treatment adherence rates. When this study commenced there were few alternatives to HRT for the prevention and treatment of

postmenopausal osteoporosis. Now that there is a wider treatment choice, regular follow-up is necessary to adjust treatment to the changing needs of women as well as conserve motivation. Such high rates of adherence to treatment, if confirmed, will entail re-evaluation of the cost-effectiveness of screening by densitometry in the field of osteoporosis prevention.

Conflict of interest D.W.P. and P.A. have received payment from pharmaceutical companies for lectures given on the menopause, osteoporosis and related subjects.

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ORIGINAL ARTICLE

Routine versus targeted vertebral fracture assessment for the detection of vertebral fractures

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Abstract
Summary Fracture risk is underestimated in women with unknown vertebral fractures. Using VFA, we compared two screening methods: targeted (6,388 women) and routine (2,176 women). Routine screening detected fractures in 20%. Targeted screening only required 5% attending for DXA to undergo VFA but only detected 9.6% of women with fractures.
Introduction BMD alone underestimates fracture risk in women with unknown vertebral fractures. We report the results of routine vertebral fracture assessment (VFA) screening and compare with targeted screening.
Method Our centre initially targeted VFA at women with reasons to suspect a vertebral fracture. Later we changed to routine VFA screening for all women over 65. We retrospectively compare each screening method's ability to detect vertebral fractures.
Results Six thousand three hundred and eighty-eight women over 65 underwent DXA during the period of targeted VFA and 2,176 during routine VFA. Routine VFA detected 420 (20.0%) women with fracture. Most vertebral fractures (56.2%) occurred in women with osteopenia. Routine VFA would be expected to alter the management of 1 in 6 osteopenic women. Targeted VFA was performed in 332 (5.2%) women detecting 122 (1.9%) women with fractures. It was estimated that targeted VFA only detected 9.6% of women with a vertebral fracture. Targeted VFA failed to detect fractures in 18.1% of the population attending for DXA and in 29% of those with osteoporosis.
Conclusion Routine VFA detects vertebral fractures in 20% of women over 65. Targeted VFA greatly reduces the number of VFAs performed but only detects a minority of the women with vertebral fractures.

Keywords Bone mineral density · Screening · Vertebral fractures · Vertebral fracture assessment

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Introduction

Vertebral fractures are the commonest osteoporotic fractures [1], are strongly associated with low bone mineral density [2, 3] and are often considered the hallmark of osteoporosis. The prevalence of vertebral fracture increases with age and in women aged over 50 the overall prevalence of vertebral fracture is 20–25% [4]. Vertebral fractures are associated with considerable morbidity [5, 6] and mortality [7]. As the number of prevalent vertebral fractures increases, the risk of suffering an incident vertebral fracture increases dramatically [8]. Furthermore, it has been demonstrated that vertebral fractures also predict future non-vertebral and hip fractures independent of bone mineral density (BMD) [9, 10]. It is therefore important to know a woman's vertebral fracture status in order to assess her risk of future fracture and guide treatment decisions. This is particularly important in osteopenic women where a prevalent vertebral fracture may make the difference between the woman receiving anti-resorptive therapy or not.

Despite the high prevalence of vertebral fractures it has been demonstrated that two thirds of women with fractures are unaware of them [4], and in these women their future fracture risk will be substantially underestimated by BMD alone. The only way to detect these asymptomatic vertebral fractures is radiologically and spinal x-rays are considered

the gold standard for vertebral fracture detection. Modern dual energy x-ray absorptiometry (DXA) scanners are able to perform a vertebral fracture assessment (VFA) of the spine which can detect vertebral fractures. Compared to spinal x-rays, VFA has the advantages of being less expensive, having a lower radiation dose and being performed at the same time as DXA [11]. VFA has been demonstrated to have a good sensitivity and specificity for vertebral fracture detection when compared to spinal x-rays [11–14]. This makes VFA a potential screening tool which can be performed on women attending for DXA.

We report the results of screening all women over the age of 65 for vertebral fractures with VFA. We aim to compare two potential screening strategies: screening all women (routine screening) and screening only those women with reasons to suspect a prevalent vertebral fracture (targeted screening). We also aim to examine the merits of routinely screening women depending on their BMD and the potential for routine screening to influence treatment decisions.

Methods

Subjects

The Centre for Metabolic Bone Disease in Hull (U.K.) is a large regional centre for bone densitometry. Since 2001 all patients attending for bone densitometry have had spine and hip BMD measured using a Lunar Prodigy bone densitometer (GE Lunar, Madison, WI). Basic patient details, including age, sex, gender and menopause age, are routinely recorded on the Prodigy's database at the time of attendance. Using this database we identified all women over the age of 65 at the time of their first DXA scan.

VFA screening method

Our centre initially adopted a targeted approach to vertebral fracture screening where women with reasons to suspect a possible fracture underwent a VFA. Indications for a targeted VFA were reported height loss (>2.5 cm, 1 inch), Dowager hump, suspected fracture on anterior-posterior spine DXA and known vertebral fracture. In August 2005 our centre changed to a routine screening program under which all women who attended for DXA underwent VFA if they were over 65 and physically able to do so.

Vertebral fracture assessment

Our centre has three Lunar Prodigy bone densitometers with VFA capability, all using software version 10.5. The scanners are subject to a rigorous quality assurance procedure, which includes weekly scanning of a purpose designed phantom for VFA [15]. The scans are performed and analysed by qualified, experienced bone densitometrists following standardised protocols.

VFA is performed with the woman positioned in the left lateral decubitus position. Initially, T4–L4 are assessed by the densitometrist for fractures using the semi-quantitative method described by Genant et al. [16]. All densitometrists are fully trained and experienced in performing VFA acquisition and evaluation. Any vertebra which are considered to be fractured subsequently undergo a six point quantitative assessment using the Prodigy computer software to measure the posterior, middle and anterior vertebral height. Fractures are graded as mild (grade 1), moderate (grade 2) or severe (grade 3) if there is a 20–25%, 25–40% or greater than 40% reduction in vertebral height, respectively. VFA has been demonstrated to correlate well with spinal x-ray for grade 2 and 3 fractures [11–13] as such these fractures are identified. Of the mild fractures detected by VFA, 50% are normal on x-ray [13]; therefore, grade 1 fractures are not identified. The VFA and DXA scan are then validated by a clinical scientist specialised in bone densitometry before the data are finally entered in to the database. A final report to the women's general practitioner is issued by an osteoporosis consultant who may also review the VFA qualitatively, but this report is not recorded on the database.

Analysis

We retrospectively identified all women over the age of 65 at the time of their first DXA scan. Depending on the screening policy at the time of attendance, women were identified as either the targeted screening group (pre-August 2005) or the routine screening group (post-August 2005). For each group, basic population demographics were determined and compared using two sample t-test or Mann–Whitney U test depending on the distribution of the data. Chi-square was used for categorical data. The routine screening group was used to determine the prevalence, type and site of vertebral fractures in our local population. Using these prevalence data, we estimated the number of women with vertebral fractures that remained undetected by targeted screening.

The routine and targeted screening groups were then divided by hip BMD at the neck of femur (NOF) into normal, osteopenic or osteoporotic. Hip BMD was used to define BMD category as this avoids the artefactual increase in spine BMD due to vertebral fracture and is the recommended site for the diagnosis of osteoporosis [17]. Using these data, we determined the number of osteopenic women in whom the knowledge of vertebral fracture status may influence the treatment decision. Finally, the number of women with vertebral fractures that remained undetected by

targeted screening for each category of BMD was estimated. Statistical analysis was performed using SPSS for Windows (version 14.0 SPSS, Inc., Chicago, IL). Our institution approved the data collection, analysis and publication.

Results

Subjects

A total of 8,564 women over the age of 65 when attending for their first DXA were identified. Six thousand three hundred and eighty-eight attended during the period of targeted VFA while 2,176 women attended during the routine screening period. The routine screening group were slightly, but significantly, older (mean age 74.3 vs. 72.5 years). The routine screening group also had a slightly older menopause age, lower hip BMD and higher spine BMD. Although these differences were statistically significant, the absolute difference between the groups for these characteristics was only 1–2%. Subject demographics are demonstrated in Table 1.

Routine VFA screening for the detection of vertebral fractures

Of the 2,176 women attending during the period of routine screening, 2,098 (96.4%) women underwent VFA. Grade 2 and 3 vertebral fractures were identified in a total of 420 women (19.3% of the population, 20.0% of VFAs) of whom 185 (44.0%) had two or more vertebral fractures (Table 2). Routine screening detected a total of 755 grade 2 and 3 vertebral fractures. Wedge and biconcave fractures were more frequent than compression fractures. Table 3 demonstrates the frequency of each type of vertebral fracture. Vertebral fractures were commonest around T7 to T9 and the thoracolumbar junction, T11–L1. Figure 1 shows the frequency of fracture at each vertebral level.

Table 1 Demographics of women over 65 attending for a DXA scan

	Targeted VFA n=6,388	Routine VFA n=2,176	Difference	p value
Age (yrs)	72.5 (5.9)	74.3 (6.1)	1.8	<0.001
Caucasian (%)	99.4	99.5	0.1	0.34
Menopause age (yrs)	46.9 (5.9)	47.6 (6.0)	0.7	<0.001
Weight (kg)	65.0 (12.8)	65.6 (14.0)	0.6	0.073
NOF BMD (g/cm2)	0.784 (0.1)	0.776 (0.1)	−0.008	0.017
Spine BMD (g/cm2)	1.021 (0.2)	1.035 (0.2)	0.014	0.006

Numbers represent mean (sd) or %

Table 2 The number of vertebral fractures detected in women undergoing routine VFA

Number of fractures	Number of women	%
0	1756	80.7
1	235	10.8
2	103	4.7
3	42	1.9
4	24	1.1
5	11	0.5
6	2	0.1
7	1	0.0
9	2	0.1
Total	2,176	100.0

Targeted VFA screening for the detection of vertebral fractures

Of the 6,388 women in the targeted group, a total of 332 (5.2%) underwent VFA resulting in the detection of 122 women with grade 2 or 3 vertebral fractures. Targeted screening resulted in a higher detection rate per VFA performed (36.7%), although only 1.9% of the total population attending for DXA had vertebral fractures detected. If it is assumed that the overall vertebral fracture prevalence rate was similar between the two groups then 1,277 women in the targeted group would have been expected to have one or more prevalent vertebral fractures on VFA. Only 122 (9.6%) of these women with fractures were detected by targeted screening leaving undetected vertebral fractures in an estimated 1,155 women, 18.1% of the population attending for DXA.

Vertebral fracture detection by category of BMD

In the targeted and routine VFA groups similar proportions of women were in the three categories of hip BMD: normal (29.7 vs. 28.7%, p=0.37), osteopenia (55.1 vs. 55.6%, p=0.70) and osteoporosis (15.2 vs. 16.6%, p=0.10). In the

Table 3 Type and severity of vertebral fractures detected in women undergoing routine VFA

	Moderate		Severe		Overall %
	n	%	n	%	
Wedge	110	14.6	191	25.3	39.9
Biconcave	142	18.8	222	29.4	48.2
Compression	51	6.8	39	5.2	11.9
Total	303	40.1	452	59.9	

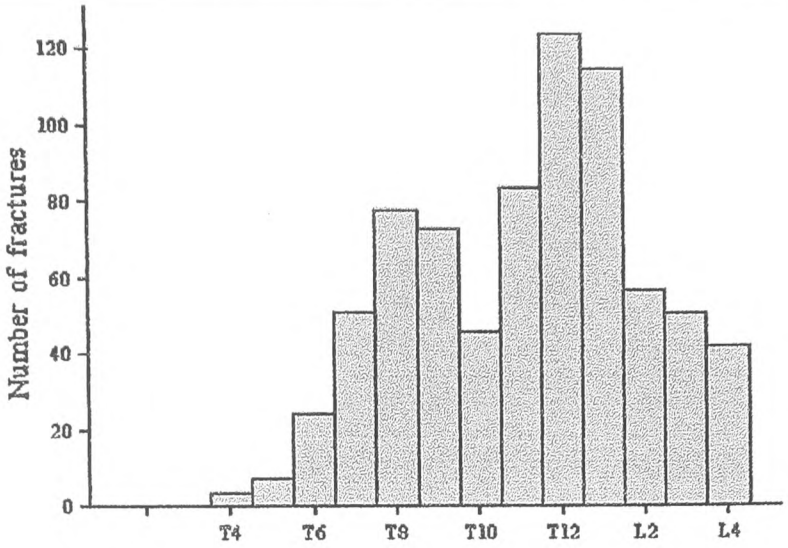

Fig. 1 Number of fractures detected at each vertebral level in women undergoing routine VFA

routine screening group, 300 of the 420 (71.4%) women with prevalent vertebral fractures did not have BMD compatible with osteoporosis. The majority of fractures occurred in women with osteopenia (236/420, 56.2%). In the routine screening group the prevalence of vertebral fractures was 10.3% of those women with normal BMD, 19.9% for osteopenic women and 33.2% in those with osteoporosis (Table 4). For the 420 women with fractures detected on VFA a history of known vertebral fracture was obtained from 8/64 (12.5%) of women with normal BMD, 53/236 (22.5%) of osteopenic women and 34/120 (28.3%) of osteoporotic women.

In the targeted screening group vertebral fractures were detected in 1.3%, 1.7% and 3.9% of the normal, osteopenic and osteoporotic women, respectively. If it is again assumed that the actual prevalence of vertebral fracture was similar between the two groups, then targeted screening underestimated vertebral fracture prevalence in each BMD category. The proportion of women with undiagnosed vertebral fractures increased with decreasing BMD: 9% of women with normal BMD, 18% with osteopenia and 29% with osteoporosis (Table 5).

Discussion

We report the actual application of VFA as a screening tool for the detection of vertebral fractures in women over 65 referred for bone densitometry. To our knowledge, this is the largest study of routine population screening with VFA, and there are no previous studies comparing routine and targeted screening methods. Vertebral fractures are common with the prevalence increasing with age from around 10% in women aged 50–59 to over 50% in those aged over 80 [4]. Furthermore, knowledge of vertebral fracture status provides important information for assessing fracture risk as prevalent vertebral fractures increase the risk of future fracture independent of BMD [9, 10]. However, despite their high prevalence and clinical relevance only one third of women with vertebral fractures are aware of them [4]. This suggests that there is a need for screening for vertebral fractures. Although thoracic and lumbar spine x-rays are the gold standard for vertebral fracture detection, VFA provides a more practical screening tool due to the lower radiation dose, lower cost and its availability at the point of service for women attending for DXA.

Table 4 Prevalence of vertebral fractures detected by VFA in each category of BMD

	BMD category[a](%)	VFA at 1st visit		Fracture on VFA		No. of fractures on VFA	
		n	%	*n*	%	Mean	Range
Targeted	Normal (29.7%)	74	3.90	24	1.27	1.67	1 to 5
	Osteopenia (55.1%)	184	5.22	60	1.70	1.55	1 to 6
	Osteoporosis (15.2%)	74	7.64	38	3.92	2.32	1 to 7
	Total	332		122		221	
Routine	Normal (28.7%)	597	95.67	64	10.26	1.34	1 to 4
	Osteopenia (55.6%)	1159	97.48	236	19.85	1.75	1 to 7
	Osteoporosis (16.6%)	341	94.20	120	33.15	2.13	1 to 9
	Total	2097[b]		420		755	

[a] BMD category relates to BMD at NOF. Spine BMD is used in cases with no data for NOF BMD (n=207)

[b] 1 woman was unable to lie supine for axial BMD although a VFA was obtained

Table 5 Estimated number of women with undiagnosed vertebral fractures despite undergoing targeted VFA

BMD category	Women with # detected	Estimated* number of women with #	No. of women with undiagnosed #	% of women with undiagnosed #
Normal, n=1,897	24	195	171	9
Osteopenia, n=3,522	60	699	639	18
Osteoporosis, n=969	38	321	283	29

*Estimate derived from the prevalence of vertebral fractures in the routine screening group

When used routinely, over 95% of women were willing and physically able to undergo VFA at our centre demonstrating that the procedure was acceptable for most women. Overall, routine screening of all women over 65 identified one woman with grade 2 or 3 vertebral fractures for every five VFAs (20%) performed, and almost half of these women had multiple fractures. The majority of fractures detected by routine screening occurred in the mid-thoracic region and thoracolumbar junction, which is consistent with previous reports using both x-ray [14, 18] and VFA [11, 16]. As with previous reports, the majority of fractures detected were wedge or biconcave [12, 19], although we found biconcave fractures to be the most common.

As would be expected, when women were divided up by BMD category, the number of women with vertebral fractures detected by routine screening increased as BMD decreased. VFA is performed after axial DXA, and as such it would be possible to perform routine VFA screening only in women with certain categories of BMD. Adopting a policy of routine VFA screening for women over 65 only if they have osteoporosis on their axial DXA would require VFA to be performed in only 16% of women and would increase the rate of vertebral fracture detection to 1 in 3 women screened. Routine VFA in this category would also allow the identification of women with the highest risk of future facture i.e., both osteoporosis and vertebral fractures [20]. However, adopting this policy would miss the majority of women with vertebral fractures as 71% of the women with vertebral fractures detected by routine screening did not have BMD compatible with osteoporosis. This confirms the findings of two smaller studies in which 60%–70% of women with vertebral fractures did not have osteoporosis [21, 22]. Furthermore, knowledge of vertebral fracture status in osteoporotic women is less likely to alter the patient's management as, over the age of 65, the majority of these women would receive treatment anyway.

Vertebral fractures may have more significant therapeutic implications in women without osteoporosis. Osteopenic women would not normally be considered for bone protective treatment based on BMD alone. The presence of a vertebral fracture would increase the risk of subsequent fracture making treatment appropriate. We found that 20% (1 in 5) of osteopenic women had vertebral fractures detected by VFA. A similar 14%–20% fracture prevalence in osteopenic women has been previously reported although direct comparison is difficult as these studies included grade 1 fractures and women less than 65 years of age [21, 22]. Only 22.5% of osteopenic women with a fracture on VFA gave a history of known vertebral fracture. Therefore, vertebral fractures were identified for the first time in 15.8% of osteopenic women suggesting that routine VFA will directly alter the management of around 1 in 6 osteopenic women. It has been demonstrated that anti-resorptive therapy is effective at reducing the risk of future fracture in women with osteopenia if they have a vertebral fracture [23, 24] and a recent analysis suggests that this treatment is cost effective [25]. Osteopenic women are most likely to benefit from routine screening with VFA given the high prevalence rate, the therapeutic and clinical implications of a vertebral fracture and the cost effectiveness of treatment.

In our population, 10% with normal BMD had vertebral fractures, which is again similar to previous reports [21, 22]. There is little evidence to suggest that bone protective treatment is of benefit or cost effective in women with normal BMD. As such the clinical relevance of finding vertebral fractures in women with normal BMD is less clear and the case for routine VFA in these women is weaker.

In addition to affecting the initial treatment decision, routine screening may also aid monitoring and future treatment decisions as it provides a pre-treatment image of the spine. This is a reference for the future from which incident fractures occurring despite treatment can be diagnosed. Osteoporotic women have the highest incidence of vertebral fracture [23], and as such routine VFA in osteoporotic women will provide valuable baseline information, even though it may not affect the initial treatment decision. Incident fractures are especially important in countries like the United Kingdom, where anabolic bone agents, such as teriparatide, can only be prescribed to women who have been proven to suffer further fractures despite treatment.

We also report the outcomes of a targeted vertebral fracture screening policy for which only women with reasons to suspect the presence of a fracture undergo a VFA. Adopting this approach to screening women over 65 greatly reduced the number of VFAs performed as only 5% of the population underwent screening. With a targeted approach 1 in 3 women undergoing VFA has vertebral fractures detected compared to 1 in 5 with routine screening. However, using the targeted approach to screening, only around 10% of women with fractures are detected. Of all the women referred for DXA during the period of targeted

VFA, 18% are estimated to have had vertebral fractures which remained undetected. The proportion of women with vertebral fractures which remain undetected increased to almost a third in women with osteoporosis. We therefore do not consider our targeted screening policy to have been effective. These figures were calculated using the assumption that the vertebral fracture prevalence was the same during the two screening periods. There were statistically significant differences between the groups in terms of age and BMD, which are risk factors for vertebral fracture. These differences may have arisen due to the non-randomised nature of this study and/or the two different time periods studied. However, the women were drawn from the same local population, from the same age group, and the difference in these factors was only 1%–2%, thus unlikely to be of clinical significance or have a major effect on fracture prevalence.

The women underwent screening as part of normal clinical practice, which, combined with the large number of women involved, means that it was not possible to confirm the VFA findings with x-rays. However, our screening program only identifies grade 2 and 3 fractures. When compared to x-ray, VFA has been reported to have a sensitivity of 80–95% for detecting grade 2 and 3 fractures and a specificity of 82%–96% for excluding vertebral fractures [12, 13, 26, 27]. Therefore, we believe that the majority of grade 2 and 3 fractures we detected were identified correctly. Our approach to screening is consistent with a recent position paper by the International Society of Clinical Densitometry which recommends that only grade 2 and 3 fractures should be identified by VFA [28].

It is well recognised that some vertebrae are uninterpretable on VFA. This can be due to poor image quality, which most frequently occurs above T7, or due to the presence of severe scoliosis or degenerative changes although similar limitations are recognised with x-ray [28]. Previous studies report that around 90–95% [12, 21, 26, 27] of vertebra are interpretable. The majority of uninterpretable vertebra occur above T7 [13, 21], where the prevalence of fracture is low, preserving the negative predictive value of VFA [14]. On our database any fractures which occurred in uninterpretable vertebra would not have been labelled as fractured, which may have reduced the number of fractures we detected. This has less of an impact when categorising women, rather than individual vertebra, as fracture or non-fracture cases. Women with fractures in uninterpretable vertebra would still be correctly classified if they also had a fracture in an interpretable vertebra. At our centre, the final report issued by the osteoporosis consultant provides an opportunity to recommend x-rays in women with uninterpretable VFAs, although these data are not available on our database.

With our screening program grade 1 fractures are not routinely identified and flagged. Previous studies have demonstrated that around one third of vertebral fractures are grade 1 fractures [12, 19], and as such this approach reduces our apparent yield from screening. This is reflected in our 20% vertebral fracture prevalence, which is lower than 33% prevalence on x-ray reported by Genant et al. [18] who included grade 1 fractures. However, this is compensated for by the increased accuracy of our screening method. Including grade 1 fractures in VFA reduces the sensitivity from 80–95% to 50–70% [12, 13, 26]. This is in part because of difficulties in differentiating mild fractures from degenerative vertebral remodelling due to the lower resolution of VFA [13]. The impact of this is minimised by our exclusion of grade 1 fractures. Grade 1 fractures may have less clinical significance. Although there is an increased risk of subsequent fracture in women with grade 1 fractures, the incidence is lower than in women with grade 2 and 3 fractures [29]. Furthermore grade 1 fractures are associated with less morbidity [30]. Again, when the VFAs and DXA scans undergo their final report by the osteoporosis consultant, possible grade 1 fractures may be identified and an x-ray recommended, but these data are not available.

We report the results of two screening programs actually used as part of normal clinical practice at our centre involving a large number of women referred for routine bone densitometry. Despite these strengths there are certain limitations. We have already discussed the lack of x-ray confirmation of fracture, the differences between the two groups and that some fractures may have remained undetected if they occurred in uninterpretable vertebra or were grade 1. Our results are only applicable to women over the age of 65. VFA screening of men or younger women would be expected to result in a lower yield as the prevalence of vertebral fracture is lower. Furthermore, we only targeted women with reasons to believe that a fracture was actually present. If our targeted screening program had also included women with risk factors for vertebral fracture, such as steroid use or prior non-vertebral fracture, then more women would have undergone VFA and a greater proportion of the women with fractures may have been detected.

Although spinal x-rays remain the gold standard for vertebral fracture detection and differentiation, VFA is a more practical screening tool for the detection of women with grade 2 and 3 fractures. Overall, routine screening results in the detection of a woman with vertebral fractures for every five VFAs performed. The majority of women with fractures have osteopenia on their axial DXA and in these women the knowledge of their fracture status may directly affect their treatment. As well as potentially

affecting the initial treatment decision, routine VFA allows better assessment of fracture risk, provides a baseline record of fracture status and can indicate the need for spinal x-rays in women with possible grade 1 fractures or uninterpretable VFA. It is possible to greatly reduce the number of VFAs performed by attempting to target screening at those women in whom there is reason to suspect a vertebral fracture; however, this only detects around 10% of women with fractures. For women over 65 who are referred for a DXA scan, routine screening for vertebral fractures with VFA is more effective than targeted screening.

Conflicts of interest None.

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The effects of short-term hormone replacement therapy on long-term bone mineral density

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Key words: BONE MINERAL DENSITY, PERIMENOPAUSE, HORMONE REPLACEMENT THERAPY

ABSTRACT

Introduction Short-term hormone replacement therapy (HRT) relieves menopausal symptoms and increases bone mineral density (BMD), but bone loss reoccurs upon discontinuation. This study assesses whether short-term HRT provides long-term BMD benefits.

Method This was a prospective study of women aged 50–54 years followed up for 9 years. Women were categorized into three groups according to the treatment they received: No-HRT ($n = 340$), Short-term HRT (2–4 years, $n = 60$), and Long-term HRT (9 years, $n = 187$).

Results BMD increased significantly at the hip (2.4%, $p < 0.001$) and spine (8.0%, $p < 0.001$) over 9 years in the Long-term HRT group. Women without treatment lost BMD at the hip (−4.2%, $p < 0.001$) and spine (−3.5%, $p < 0.001$). Women in the Short-term HRT group had no significant loss of BMD at the hip (−1.6%, $p = 0.08$) or spine (−1.4%, $p = 0.18$) over 9 years. BMD in the Short-term HRT group was significantly higher at 9 years than in the No-HRT group at both spine (difference 0.023 g/cm^2, $p = 0.048$) and hip (difference 0.016 g/cm^2, $p = 0.042$).

Conclusion After 9 years, women who had taken short-term HRT had no significant loss of BMD and were better off in terms of BMD than those left untreated. Short-term HRT in the early postmenopausal period provides long-term BMD benefits.

INTRODUCTION

Previously, hormone replacement therapy (HRT) was the cornerstone of osteoporosis treatment in women. In 2002, the Women's Health Initiative (WHI) study confirmed that HRT, taken for an average of 5.6 years, was indeed effective in preventing osteoporotic fractures overall and specifically of the hip[1,2]. Unfortunately, these benefits were offset due to an increased incidence of breast cancer and vascular events[2]. This, combined with the advent of other effective treatments for osteoporosis, resulted in long-term HRT no longer being considered an appropriate treatment option for osteoporosis. Bisphosphonates are now first-line therapy, although HRT is still licensed for short-term use around the time of the menopause for the relief of menopausal symptoms.

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Bisphosphonates are effective treatments for osteoporosis, but, lately, concerns have been expressed regarding their efficacy and safety in the long term[3]. If there are concerns about long-term bisphosphonates, how should we treat osteoporotic women in their fifties who potentially require 30–40 years of treatment? As HRT does not have the prolonged effects on bone seen with bisphosphonates[4], one option may be initially to use a short course of HRT. However, when HRT is stopped, bone mineral density (BMD) decreases and the long-term effects on bone of short-term HRT have not been fully established.

The aim of this study is to investigate whether women who take short-term HRT around the time of the menopause have long-term gains in their BMD compared to those who take no treatment.

METHODS

Background

In the 1990s, the Centre for Metabolic Bone Disease at Hull Royal Infirmary commenced a feasibility study to investigate the logistics of population screening for osteoporosis[5]. All women in the local area aged 50–54 years were invited by letter for a BMD assessment by dual-energy X-ray absorptiometry (DXA) of the spine and hip using a Lunar DPX-L densitometer (GE Lunar, Madison, WI, USA). The only exclusions from screening were terminal illness, weight in excess of 125 kg and physical inability to comply with the standard DXA scanning technique. Information was collected regarding menopause age, medical conditions, family history, smoking status, fractures and medications.

Treatment

As this study commenced prior to the World Health Organization definition of osteoporosis, women were deemed 'at risk' if their BMD was in the lowest quartile for their age-matched population. These women were recommended for treatment with HRT, the bone-protective treatment of choice at the time for the early postmenopausal period. The subject's general practitioner (GP) made the final choice of HRT preparation from a list of HRT regimens then known through interventional studies to be osteoprotective. Thus, treatment regimens contained either 2 mg estradiol, 0.625 mg conjugated equine estrogen or a 50 μg transdermal patch. Progesterone was prescribed to women with a uterus.

Follow up

Those women considered at risk, and an equal number of randomly selected women not recommended for treatment, were invited back for repeat assessment 2, 5 and 9 years later. Patients were free to stop or change therapy under the guidance of their GP in between visits. Patients were blinded to the 2-year scan results. As such, those discontinuing HRT early did so due to intolerance rather than BMD changes; full reasons for discontinuation are described in the original study[5]. At each follow-up visit, a medical history was taken documenting general health, medications (including HRT) and clinical fractures. A repeat DXA was performed using the same DXA machine as for the baseline visit. All details were recorded on the database at our Centre.

Subjects for present analysis

The present analysis uses all women who were followed up for 9 years after the screening program. From the database, we identified all women who could be allocated to one of three groups: those who took no HRT (No-HRT group); those who took 24–48 months of HRT prior to the 5-year visit with no subsequent HRT use (Short-term HRT group); and those who took at least 8.5 years of HRT during the 9-year follow-up period (Long-term HRT group). The only exclusion criteria were the use of bisphosphonates or raloxifene before or during the follow-up period, and not meeting the above HRT treatment group requirements. Calcium supplementation was permitted. The duration of treatment chosen for the Short-term HRT group was selected to represent patients who had received HRT for enough time to be able to detect a change in BMD (2 years) but less than the time taken for the incidence of breast cancer to differentiate from placebo in the WHI study[2]. The discontinuation rates and the reason for HRT discontinuation for this cohort of patients have previously been reported[5,6].

The primary end-point was the difference in BMD at 9 years at the spine (L2–4) and hip (neck of femur) in the No-HRT group compared to the Short-term HRT group. The primary analysis was carried out on these two groups only, as long-term HRT is no longer a treatment option and the aim of the study was to compare short-term HRT to no treatment. Secondary end-points were change in BMD over 9 years within each group (intragroup analysis) and fracture rates in the No-HRT and Short-term HRT groups.

The local ethics committee approved both the original screening program and the present analysis of the 9-year data.

Statistical analysis

Baseline characteristics were analyzed using a one-way analysis of variance (ANOVA) for continuous data and Pearson's χ^2 test for categorical data. Means within groups were compared using a paired t test. A Multivariate General linear model adjusted by covariates (Multivariate ANCOVA) was used to examine the effect of treatment after 9 years of follow-up on the dependent variables and to obtain adjusted means; the dependent variables were Spine BMD and Neck of femur BMD measured after 9 years' follow-up; covariates were Spine BMD and Neck of femur BMD at baseline. Bonferroni adjustment for multiple comparisons was made. A χ^2 test or a Fisher exact test was performed to test the association between Fractures and HRT. The significance level chosen was 0.05. The program package used was SPSS for Windows (version 12.5 SPSS, Inc., Chicago, IL, USA).

RESULTS

A total of 1303 women were on the database and had been followed up for 9 years; 125 women were excluded due to bisphosphonate use. Of the remaining 1178 women, a further 591 women were excluded due to HRT use incompatible with the required groups. Finally, 587 (49.8%) women could be allocated to one of the three groups: 340 No-HRT (57.9%); 60 Short-term HRT (10.2%); and 187 Long-term HRT (31.9%). Relevant characteristics of each group are shown in Table 1. The mean (standard deviation) duration of HRT use was 34.7 (8.5) months in the Short-term HRT group and 107.4 (2.3) months in the Long-term HRT group. There was no significant difference in the mean age when starting HRT (52.6 and 52.4 years, respectively, $p = 0.76$)

Intragroup analysis

The absolute 9-year changes in BMD in each group are shown in Table 2 and the percentage changes from baseline at each visit are shown in Figures 1 and 2. Over the 9-year period, those treated with long-term HRT sustained a significant increase in BMD at the spine (+8.0%, $p < 0.001$) and hip (+2.4%, $p < 0.001$). Those not taking HRT lost a significant amount of BMD at the spine (−3.5%, $p < 0.001$) and hip (−4.2%, $p < 0.001$). Despite a downward trend, the Short-term HRT group had no significant change in BMD over the 9 years at the spine (−1.4%, $p = 0.18$) or hip (−1.6%, $p = 0.08$). There was no significant difference in weight gain between the three groups to confound the measurement of BMD (No-HRT +3.6 kg, Short-term HRT +3.8 kg, Long-term HRT +3.6 kg; $p = 0.97$).

Intergroup analysis

The BMDs in the No-HRT group and the Short-term HRT group were compared after adjusting for the difference in baseline BMD. At 9 years, those women taking short-term HRT had a significantly higher spinal BMD than those taking no HRT (adjusted BMD: 1.091 g/cm^2 vs. 1.068 g/cm^2; $p = 0.048$). The hip (neck of femur) BMD was also significantly higher in the Short-term HRT group (0.865 g/cm^2 vs. 0.849 g/cm^2; $p = 0.042$).

Fractures

All fracture types were grouped together for analysis, as the sample populations were too small

Table 1 Baseline characteristics. Values are expressed as mean (standard deviation) or n (%)

	No HRT ($n = 340$)	*Short-term HRT* ($n = 60$)	*Long-term HRT* ($n = 187$)	*p Value*
Age (years)	52.5 (1.4)	52.5 (1.33)	52.3 (1.4)	0.50
Weight (kg)	67.1 (10.6)	63.5 (9.6)	61.8 (9.8)	<0.001*
Menopause age (years)	49.3 (4.7)	49.1 (3.6)	47.3 (4.7)	<0.001*
Family history (%)	38 (11.2)	15 (25)	30 (16)	0.06
Current smoking (%)	98 (28.8)	23 (38.3)	69 (36.9)	0.098
Alcohol (units/week)	2.4 (3.5)	2 (3)	2.3 (3.3)	0.72
BMD spine (g/cm^2)	1.110 (0.16)	1.060 (0.12)	1.002 (0.12)	<0.001*
BMD NOF (g/cm^2)	0.893 (0.11)	0.836 (0.09)	0.820 (0.09)	<0.001*

*$p < 0.05$; BMD, bone mineral density; NOF, neck of femur

to allow specific fracture sites to be compared. In the No-HRT group, 54 (15.9%) women suffered a total of 64 fractures compared to six (11.7%) women suffering a total of seven fractures in the Short-term HRT group. After 9 years, there was a lower incidence of fractures in the Short-term HRT group compared to the No-HRT group, although this was not statistically significant (relative risk (RR) = 0.51, 95% confidence interval (CI) 0.16–1.62; $p = 0.35$). Logistic regression was used to correct for the baseline differences in spinal BMD. Correction for baseline BMD had little effect on the observed fracture incidence with short-term HRT (RR = 0.46, 95% CI 0.14–1.57; $p = 0.22$).

Table 2 Intragroup analysis

	No HRT	*Short-term HRT*	*Long-term HRT*
BMD spine			
Year 1	1.114	1.059	1.002
Year 9	1.075	1.044	1.084
Mean change (g/cm^2)	−0.039	−0.015	0.081
Percentage change	−3.514	−1.415	7.976
p Value	<0.001*	0.18	<0.001*
BMD NOF			
Year 1	0.893	0.836	0.820
Year 9	0.856	0.822	0.840
Mean change (g/cm^2)	−0.037	−0.013	0.020
Percentage change	−4.157	−1.566	2.439
p Value	<0.001*	0.08	<0.001*

*$p < 0.05$; BMD, bone mineral density; NOF, neck of femur

DISCUSSION

The WHI study has confirmed the bone-protective effects of HRT, with a 33% reduction in hip fracture[1], but this is offset, in women taking combined HRT preparations, by an increase in vascular events and breast cancer[2]. The increase in breast cancer was not apparent until after 4 years of treatment[2] and hence HRT is still licensed for short-term use for the relief of menopausal symptoms. The present study suggests that women who take between 2 and 4 years of HRT in the early postmenopausal period have a prolonged benefit in terms of BMD, as, 4–5 years after discontinuing HRT, they had a higher BMD than the non-users. Furthermore, over 9 years, there was no significant loss of BMD in short-term HRT users. This study also demonstrated a

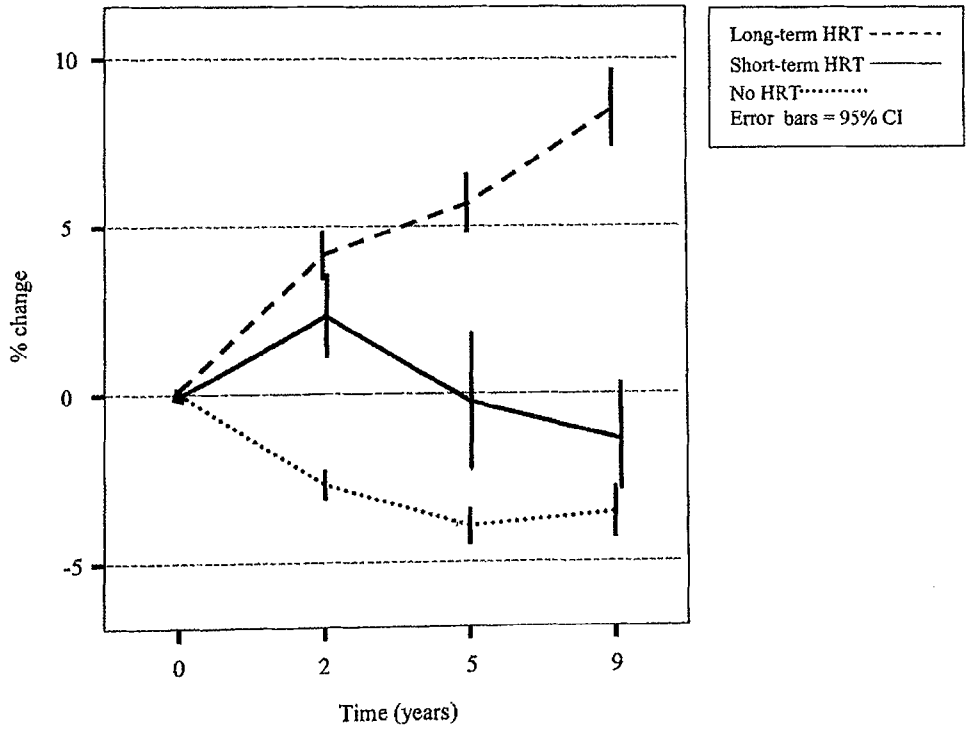

Figure 1 Percentage change in spine bone mineral density (BMD) from baseline

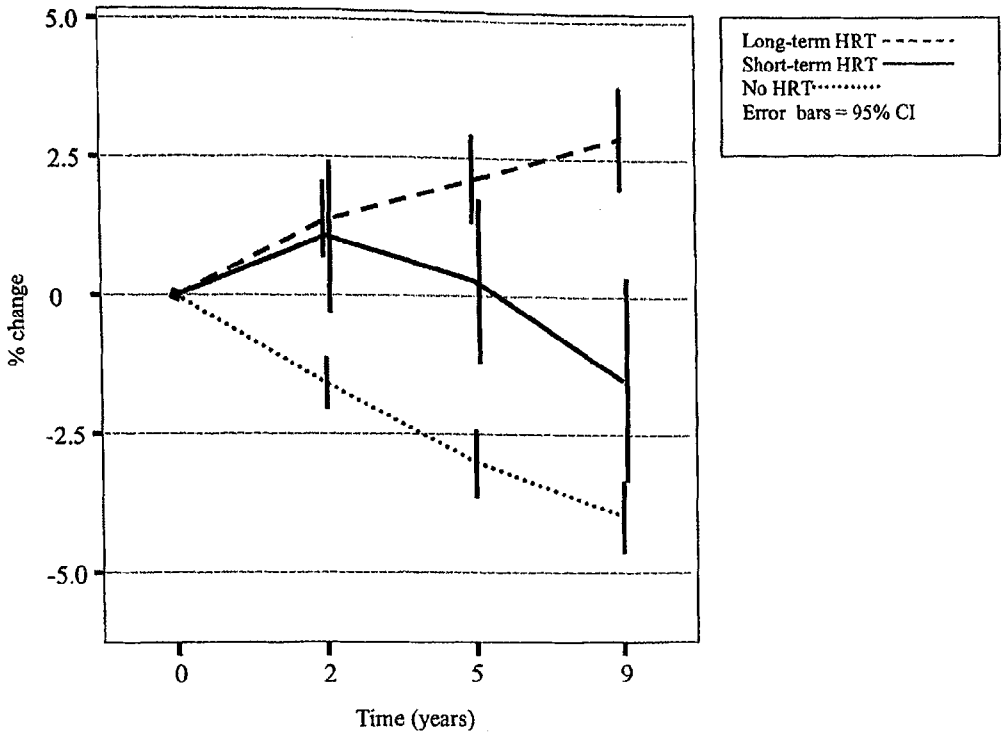

Figure 2 Percentage change in bone mineral density of neck of femur from baseline

lower incidence of fractures associated with short-term HRT use. This did not reach significance, although the study was underpowered to detect a difference in fracture rates. Short-term HRT has previously been demonstrated to reduce the risk of all fractures in early postmenopausal women by 52%[7]. The present study demonstrated a similar magnitude of fracture reduction.

Short-term HRT may have a role to play in the overall treatment strategy for women with low BMD during the early postmenopausal period. Recently, concerns have been raised regarding the long-term safety and efficacy of bisphosphonates[3]. The 10-year data for alendronate from the FLEX trial suggest that there are no benefits in continued treatment beyond 5 years in terms of non-vertebral fractures or morphometric vertebral fractures[8]. A smaller 10-year study also demonstrated that stopping alendronate at 5 years resulted in little difference in terms of vertebral fracture compared to continuing alendronate[9]. Of more concern is the possibility of harm due to long-term bisphosphonates. Osteonecrosis of the mandible has been repeatedly reported[10,11]. A recent paper reported a series of patients, with low trauma fractures occurring after long-term bisphosphonates, who had severely suppressed bone turnover on bone biopsy[12]. Animal models also demonstrate microdamage accumulation with bisphosphonate exposure[13]. If there are concerns about long-term bisphosphonate use, what treatment should be offered to women with low BMD in their fifties who are at risk of developing osteoporosis and require a treatment strategy for the next 30–40 years? BMD will continue to decline if treatment is delayed, as in the No-HRT group in this study. Raloxifene could be used if the site of concern is the spine, but this could exacerbate the menopausal symptoms common in the early postmenopausal period and has no proven benefits in terms of non-vertebral fractures[14]. Our study suggests that short-term HRT in the early menopausal period may provide both relief of menopausal symptoms and preservation of BMD, thus allowing bisphosphonate therapy to be delayed.

One previous paper by Bagger and colleagues[7] has examined the effects of short-term HRT in the early menopausal period. As in the present study, those women treated with short-term HRT had long-term benefits in terms of BMD, and this study also demonstrated a significant reduction in both vertebral and all-fractures. The women in both studies were of similar age and in the early postmenopausal period but there are several differences in the methodology. Bagger and colleagues

amalgamated four randomized, controlled trials in which only otherwise healthy women were recruited and set treatment regimes were used. Our study was an observational one in which the general population was screened, appropriate clinical advice regarding treatment was given and the women were free to change or stop their HRT under their GP's guidance. As such, our study is more representative of real clinical practice and suggests that the benefits of short-term HRT predicted by Bagger and colleagues still occur when an unselected population is studied. This is important as recent studies have demonstrated how patient selection can bias the characteristics of study populations[15,16]. Bagger and colleagues also had to use different models of DXA scanner throughout their study, thus requiring the use of a conversion factor, whereas, in our study, each patient was scanned on the same machine at each visit, allowing direct comparison. We also prospectively followed up the patients at 2, 5 and 9 years, whereas Bagger and colleagues followed up all patients at one point in time, either 5, 11 or 15 years after the end of their original trial.

There are limitations to our study. Women were treated as clinically indicated and were not randomized to each treatment arm. Although this mirrors clinical practice, it resulted in significant differences between the groups at baseline in terms of BMD, weight and menopause age. This is largely expected as women with an earlier menopause and lower weight are more likely to have a lower BMD, be recommended for treatment and persist with the treatment for longer. It is interesting to note that, compared to the No-HRT group, the Short-term HRT group had a lower weight and higher prevalence of smoking. These factors are associated with an increased rate of BMD loss[17,18], yet, in spite of this, the Short-term HRT group lost less BMD over the 9 years. Any effect these factors had on the present analysis should be to increase the BMD loss in the Short-term HRT group, thus making our results conservative. Finally, despite having a low BMD for their age, the women in this study were not osteoporotic by the WHO definition. t Scores at baseline were -0.75 and -1.17 in the No-HRT group and Short-term HRT group, respectively. Bagger and colleagues[7] also looked at women with normal BMD and, as such, there are no studies assessing the effect of short term HRT on osteoporotic women in the early post-menopausal period.

When considering HRT, it is important to balance the benefits of treatment with the risks of vascular disease and breast cancer. The type of HRT required also needs consideration as estrogen-only HRT, recently confirmed to provide fracture protection[19], does not have the increased incidence of coronary heart disease and breast cancer associated with combined HRT[20]. Clearly, HRT is not a suitable treatment option for all patients. However, for women with low BMD in the early menopausal period, short-term HRT may provide a useful initial treatment option and have lasting benefits.

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Conflict of Interest Nil.

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APPENDIX V

Raising of standards through education and guidance

National Training Scheme *for* Bone Densitometry

The only formal certification scheme for competence in bone densitometry in the UK

Approved by the College of Radiographers (COR) and the Institute of Physics and Engineering in Medicine (IPEM)

Visit www.nos.org.uk for more information

Theoretical Lecture Course on Osteoporosis and Bone Densitometry
16th & 17th March, 2009 – Novotel, Birmingham Centre

The lecture course is open to all health professionals with an interest in osteoporosis and bone densitometry e.g. physicians, nurses, radiographers, technologists or clinical scientists

Day 1: Core Module: Introduction to Osteoporosis and Bone Densitometry

An educational update:

- Epidemiology and pathophysiology of bone
- Diagnosis, treatment and prevention of osteoporosis
- Overview of methods for bone densitometry
- How to run a densitometry service
- Clinical interpretation and reporting of bone density measurements

Day 2: DXA / pDXA (morning)

An in-depth look at:

- The techniques of axial and peripheral dual energy x-ray
- absorptiometry (DXA)
- Special applications of bone densitometry
- Quality control, quality assurance, errors and artefacts

Day 2: Radiation Protection IR(ME)R 2000 (afternoon)

- Radiation hazards and dose
- Patient and staff protection
- Statutory requirements and legislation

Certification

Certification is aimed at healthcare professionals who operate bone densitometry equipment in the UK.

3 steps to certification:

1. attend the lecture course plus the IR(ME)R course (unless this training has already been acquired) (March 2009)
2. pass the examination (taken online at regional centres) (Summer 2009)
3. submit a portfolio of work demonstrating competence in your chosen method of bone densitometry (Autumn 2009)
4. upon successful completion of all three elements a Certificate of Competence is awarded.

The National Training Scheme for Bone Densitometry is approved by the College of Radiographers and the Institute of Physics and Engineering in Medicine (IPEM).

Candidates wishing to pursue certification must have 6 months full time or 12 months part time scanning experience, be employed in clinical practice and have received local training.

The Training Scheme Rules and Regulations are available at www.nos.org.uk

Registration for Lecture Course

To register, complete the form overleaf and return with payment to: The Training Scheme Administrator, National Osteoporosis Society, Camerton, Bath, BA2 0PJ, Tel: 01761 473132 Fax: 01761 471104.
Website: www.nos.org.uk Email: courses@nos.org.uk

Closing date for registration is 25th February 2009

National Osteoporosis Society

Lecture Course Registration Form

PLEASE COMPLETE IN BLOCK CAPITALS

SURNAME (Dr/Mr/Mrs/Ms) ..... FIRST NAME.....

EMPLOYMENT ADDRESS

JOB TITLE..... ORGANISATION.....

ADDRESS .....

.....POSTCODE .....

DAYTIME TELEPHONE ..... DAYTIME FAX .....

EMAIL.....

CORRESPONDENCE ADDRESS (IF DIFFERENT FROM ABOVE).....

.....

..... POSTCODE .....

PLEASE DELETE AS APPROPRIATE (please complete all sections)

I HAVE/HAVE NOT READ THE RULES & REGULATIONS, AND DO/DO NOT INTEND TO SEEK CERTIFICATION

I HAVE/HAVE NOT RECEIVED LOCAL TRAINING IN ONE OR MORE TECHNIQUES OF BONE DENSITOMETRY

I AM/AM NOT CURRENTLY EMPLOYED IN CLINICAL PRACTICE

I WILL/WILL NOT HAVE 6 MONTHS FULL TIME OR 12 MONTHS PART TIME SCANNING EXPERIENCE BY 16/03/2009

I WOULD LIKE TO REGISTER FOR THE FOLLOWING (PLEASE TICK)

	NATIONAL OSTEOPOROSIS SOCIETY PROFESSIONAL MEMBER [1]		REDUCED FEE[2,3]		STANDARD FEE[3]	
CORE MODULE (one day)	£165	☐	£195	☐	£225	☐
DXA/pDXA MODULE (half day)	£125	☐	£140	☐	£175	☐
RADIATION PROTECTION IR(MER) (half day)	£125	☐	£140	☐	£175	☐

[1] National Osteoporosis Society Professional member number: .....

[2] The reduced fee is available to all NHS employees, university employees and students.

[3] All those who pay the reduced or standard fee will automatically receive *6 months free Professional Membership* of the National Osteoporosis Society, which entitles you to a range of benefits including reduced fees for the National Osteoporosis Conference and copies of 'Osteoporosis Review'. To find out more about membership call 01761 473118.

Registration fees include lunch, refreshments, Fundamentals of Bone Densitometry CD ROM and course folder.

** Additional fees apply for the examination and portfolio submission – available from www.nos.org.uk **

Please list any dietary or access requirements you have.....

If you are attending the IR(ME)R module, please state whether you will require a Practitioner's or Operator's certificate:-

☐ PRACTITIONER ☐ OPERATOR

I ENCLOSE A **CHEQUE** FOR A TOTAL OF £.....

PLEASE MAKE ALL CHEQUES PAYABLE TO **NATIONAL OSTEOPOROSIS SOCIETY**

I WISH TO PAY BY DEBIT OR CREDIT CARD – PLEASE DEBIT MY VISA/MASTERCARD £.....

VISA/MASTERCARD NUMBER..... VALID FROM ..... EXPIRY DATE.....

ISSUE NUMBER .....SIGNATURE OF CARDHOLDER ..... TODAY'S DATE.....

Cancellation policy: 30+ days notice - 80% refund, 15-29 days - 50% refund, 14 days or less - no refund. Registration is non-transferable.

☐ The National Osteoporosis Society may contact you to keep you informed of future appeals and promotions. If you are NOT happy to be contacted, please tick this box.

RULES AND REGULATIONS

1. Overview

1.1 The National Osteoporosis Society is the only UK national charity dedicated to improving the prevention, diagnosis, and treatment of osteoporosis. As part of our work we aim to ensure that the different strands of people working with osteoporosis patients have adequate information and training to meet patient needs.

1.2 The Bone Densitometry Certification Panel (BDCP) is a group of voluntary Scientific Advisors who are responsible for overseeing the National Training Scheme for Bone Densitometry. The Bone Densitometry Certification Panel reports to the charity's Medical Board.

2. Aim

2.1 The National Training Scheme for Bone Densitometry ('the Training Scheme') provides an accredited scheme, recognised by the appropriate professional colleges and institutions, that offers an opportunity for bone densitometry operators to demonstrate their competency. In doing so it is hoped that consistently high standards in bone densitometry are achieved across the UK.

2.2 Successful completion of the Training Scheme leads to certification by the National Osteoporosis Society. This offers proof of competence to perform clinical bone densitometry measurements in the applicant's chosen bone densitometry technique(s).

3. Approval

3.1 The content of the Training Scheme has been approved by the Institute of Physics and Engineering in Medicine (IPEM)[1] and the College of Radiographers (COR) which represent the majority of healthcare professionals involved in clinical bone densitometry in the UK. Their recognition ensures that professional standards of teaching and examination are maintained.

4. Eligibility for certification

4.1 The Training Scheme is aimed at healthcare professionals who are currently employed in clinical bone densitometry practice and are:

- State registered healthcare professionals

Or

- Healthcare professionals or graduate scientists working in clinical practice under the supervision of a registered practitioner

All applicants must also have received local training in one or more techniques of bone densitometry and have had at least 6 months full-time or 12 months part-time (minimum 1 whole day per week) scanning experience at the time of the lecture course.

4.2 Any applicant not meeting the above criteria should complete a Certification Admission Appeal Form, available from the National Osteoporosis Society, and include a copy of their CV. The Bone Densitometry Certification Panel will consider such applications on a case-by-case basis.

4.3 The National Osteoporosis Society reserves the right to refuse an applicant entry to the certification process at its absolute discretion.

[1] Currently applying for renewal for approval of IR(ME)R course

5. Admission requirements for certification

5.1 Applicants must complete a registration form, which will require details of previous training and experience relevant to bone densitometry.

5.2 Applicants must attend the lecture course which comprises: 'Core Module' and 'DXA/pDXA Module' (1 1/2 days).

5.3 In addition, all applicants who have not already received professional training according to the requirements of IR(ME)R 2000 are required to attend the charity's IR(ME)R course, held on the afternoon following the lecture course.

5.4 Evidence of IR(ME)R certification will be required from applicants who have completed a course delivered by another training body.

6. Exemptions

6.1 In the absence of an equivalent accredited training scheme in bone densitometry in the UK, no exemptions are available for this Training Scheme.

7. Certification Process

7.1 Full attendance at the lecture course (plus the IR(ME)R course as appropriate) is compulsory for all candidates pursuing certification.

7.2 Candidates must pass both examination modules prior to submission of a portfolio relating to their densitometry specialty.

7.3 A portfolio must be submitted by the agreed deadline.

7.4 Candidates must achieve a pass mark for both the examination and the submitted portfolio to achieve certification.

7.5 If a candidate fails to achieve a pass mark for the examination they can apply to re-sit the examination. Failure at the third attempt will require the candidate to attend the lecture course for a second time before re-sitting the examination.

7.6 Resubmission of failed portfolios:

7.6.1 If a candidate achieves a satisfactory pass mark in at least one of the four portfolio sections at their first attempt, they will be permitted two resubmissions of the failed sections.

7.6.2 If a candidate fails all four sections at the first attempt they will be permitted one resubmission of the complete portfolio. Candidates passing at least one section at a second attempt will be permitted to have one final attempt at the failed sections. Candidates failing all four sections at a second attempt will be advised to attend the lecture course again before having one final opportunity to submit a portfolio.

7.6.3 In none of the above circumstances will a candidate be asked to retake the examination.

7.6.4 All submissions must be made by the relevant dead-line set by the National Osteoporosis Society.

7.7 The National Osteoporosis Society reserves the right to refuse certification to individuals who failed to meet the required criteria, at its absolute discretion.

8. Fees and cancellation

8.1 Course fees are payable in three parts: lecture course, examination and portfolio. Places are only guaranteed on receipt of payment. Payments must be made by the registration deadlines.

8.2 All cancellations must be made in writing. Cancellation charges are as follows:
Over 30 days notice before the date of the lecture course/exam/portfolio submission deadline - 80% refund;
15 to 29 days notice – 50% refund;
14 days notice or less – no refund.

8.3 Registration is non-transferable.

8.4 If payment is not received by the date of the lecture course we reserve the right to make an additional administration charge of £50 per delegate.

8.5 All fees for the Training Scheme must have been paid in full before candidates are entitled to receive certification.

February 2009

National Training Scheme for Bone Densitometry

National Osteoporosis Society

Programme:
Monday 16th March: Core Module

8.30 am	**Registration and Refreshments**
9.30 am	**Welcome and Introduction** Professor Francis Ring, Bone Densitometry Certification Panel
9.45 am	**Pathophysiology of Bone** Professor Roger Francis, Consultant Physician, Freeman Hospital, Newcastle upon Tyne
10.15 am	**Epidemiology of Osteoporosis** Professor Roger Francis, Consultant Physician, Freeman Hospital, Newcastle upon Tyne
10.45 am	**Questions**
11.00 am	**Refreshment Break**
11.20 am	**Diagnostic Assessment of Osteoporosis** Professor Judith Adams, Clinical Academic Group Leader, Department of Diagnostic Radiology, University of Manchester
11.50 am	**Prevention and Treatment of Osteoporosis** Dr Nicky Peel, Consultant in Metabolic Bone Medicine, Sheffield Teaching Hospitals NHS Foundation Trust
12.20 pm	**Questions**
12.30 pm	**Lunch**
1.30 pm	**Overview of Methods and Instruments for Bone Densitometry** Dr Wil Evans, Consultant Physicist, University Hospital of Wales, Cardiff
2.00 pm	**Overview of the Bone Densitometry Service** Ms Sue Steel, Consultant Physicist, Hull & East Yorkshire Hospitals Trust
2.30 pm	**Terminology Used in Bone Mass Measurement** Dr Karen Knapp, Senior Lecturer, School of Physics, University of Exeter
2.45 pm	**Questions**
3.00 pm	**Refreshment Break**
3.30 pm	**Clinical Interpretation and Reporting of BMD Results** Dr Nicky Peel, Consultant in Metabolic Bone Medicine, Sheffield Teaching Hospitals NHS Foundation Trust
4.15 pm	**Questions**
4.30 pm	**Certification Procedures: Eligibility, Examination and the Portfolio** Hilary McWilliam, Clinical Training Officer, National Osteoporosis Society
5.00 pm	**Questions & Comments to the Bone Densitometry Certification Panel**
5.30 pm	**Finish**

National Training Scheme for Bone Densitometry

National Osteoporosis Society

Programme:
Tuesday 17th March: DXA/pDXA Module

8.30 am	**Refreshments**
8.45 am	**Principles of Dual Energy X-Ray Absorptiometry (DXA)** Ms Sue Steel, Consultant Physicist, Hull & East Yorkshire Hospitals Trust
9.05 am	**Techniques of Axial DXA** Dr Karen Knapp, Senior Lecturer, School of Physics, University of Exeter
9.50 am	**Techniques of Peripheral DXA** Dr Rajesh Patel, Head of Academic Bone Densitometry & Clinical Studies, Imperial College, London
10.10am	**Special Applications: Total Body DXA, Vertebral Fracture Assessment and Bone Densitometry in Children and Young Women** Dr Glen Blake, Consultant Physicist, Guy's Hospital, London
10.40 am	**Refreshment Break**
11.00 am	**Questions**
11.10 am	**Errors and Artefacts in DXA and pDXA** Professor Francis Ring, Director of Medical Imaging Research Unit, Faculty of Advanced Technology, University of Glamorgan
11.35 am	**Quality Control, Quality Assurance, Commissioning and Radiation Protection for DXA** Dr Rajesh Patel, Head of Academic Bone Densitometry & Clinical Studies, Imperial College, London
12.15 pm	**Questions**
12.30 pm	**Lunch**

Radiation Protection
IR(ME)R 2000 Course

National Osteoporosis Society

Programme:
Tuesday 17th March 2009

1.30 pm	**Introduction** Dr David Pye, Radiation Protection Advisor, Nottingham University Hospitals NHS Trust
1.45 pm	**The Use of X-Rays in Bone Densitometry** Dr Wil Evans, Consultant Physicist, University Hospital of Wales, Cardiff
2.30 pm	**Radiation Hazards and Radiation Dose** Dr Glen Blake, Consultant Physicist, Guy's Hospital, London
2.50 pm	**Statutory Requirements and Legislation** Dr Wil Evans, Consultant Physicist, University Hospital of Wales, Cardiff
3.20 pm	**Questions**
3.30 pm	**Refreshment Break**
4.00 pm	**Radiation Protection of Patients** Dr David Pye, Radiation Protection Advisor, Nottingham University Hospitals NHS Trust
4.45 pm	**Radiation Protection of Staff** Dr Glen Blake, Consultant Physicist, Guy's Hospital, London
5.15 pm	**Questions**
5.30 pm	**Finish**

National Training Scheme
for Bone Densitometry

National Osteoporosis Society

SYLLABUS

The Training Scheme Syllabus comprises two compulsory modules: Core Module and DXA/pDXA Module. All applicants who have not already received professional training according to the requirements of IR(ME)R 2000 are also required to attend the IR(ME)R course (syllabus overleaf).

Core Module Syllabus

Pathophysiology of bone

- Definitions of osteoporosis
- Skeletal structure, peak bone mass, bone remodelling
- Aetiology of osteoporosis
- Clinical consequences of osteoporosis

Epidemiology of osteoporosis

- Incidence of osteoporosis in men and women
- Pattern of fracture incidence
- Contribution of BMD to fracture risk
- Morbidity and mortality related to fracture

Diagnostic assessment of osteoporosis

- Indications for bone densitometry
- Diagnostic evaluation of osteoporosis
- Radiology
- Bone density measurements
- Blood and urine tests, bone biopsy, bone markers

Treatment and prevention of osteoporosis

- Prevention versus treatment
- Drugs to improve bone mass
- Bisphosphonates, SERMS, parathyroid hormone, Calcium & vitamin D
- Anabolic agents
- Non-drug interventions to reduce fracture risk
- Lifestyle modification
- Prevention of falls and trauma

Overview of methods and instruments for bone densitometry

- Physical principles of X-radiation and ultrasound
- Quantities to measure: attenuation and velocity
- Nature of X-rays: waves and photons, X-ray spectrum
- X-ray attenuation: absorption and scatter
- X-ray absorptiometry: bone mineral, soft tissue, area density
- SXA: Average photon energy, peripheral sites, BMC, BMD
- DXA: spectrum modification, axial sites, BMC and BMD
- QCT: slice reconstruction, CT numbers, BMD
- Nature of ultrasound: longitudinal waves, continuous/pulsed
- QUS velocity: bone length, ultrasound transit time
- QUS attenuation: broadband pulse, frequency dependence, BUA
- BMD vs. surrogate quantities

Overview of the bone densitometry service

- Procedures and Organisation: accommodation, referral guidelines, request receipt, appointment, questionnaires, patient handling, reporting, clinics
- Protocols and Equipment: written procedures, quality control, data collection and audit, scan procedures, archiving, equipment maintenance, safety, radiation protection, choice of equipment
- Staffing: operators, scientific support, clinical, clerical, reception, nursing, Radiation Protection Advisors (RPAs)
- Example of 'best practice'

Terminology used in bone mass measurements

- Commonality of terms between the different technologies
- Explanation and calculation of BMD and BMC, areal and volumetric ionising radiation techniques
- Standardised BMD and its use
- Explanation of U/S terminology
- Reference ranges: collection, causes for differences between populations/scanners, NHANES III database
- Adjustments for race and weight
- Comparison of the use of scores between the BMD technologies

Clinical interpretation and reporting of BMD results

- Relationship between BMD and fracture risk
- Site-specificity
- Technique used
- Definition of osteoporosis and osteopenia
- WHO criteria
- Independent risk factors for fracture
- Principles of reporting
- Technical, clinical
- Management and follow-up

DXA/pDXA Module Syllabus

Principles of Dual Energy X-ray Absorptiometry (DXA)

- Principal components of a DXA system
- DXA detectors: scintillation, solid state, energy discrimination
- Differential attenuation in bone and soft tissue
- Use of appropriate scan modes
- Determination of BMD: empirical, mathematical
- Beam geometry: pencil beam, fan beam, cone beam

Techniques of Axial DXA

- Patient preparation – prior to scan appointment and at the appointment
- Pregnancy status for ionising radiation techniques- IRMER
- Previous examinations – barium studies/ IV contrast/ radionuclide imaging
- Patient measurements – weight/ height: forearm length
- Aftercare of patient
- DXA – Lumbar spine (PA and Lat): positioning, acquisition and analysis (differences between Hologic & GE-Lunar)
- Problems in spinal analysis
- DXA – Proximal femur: positioning, acquisition and analysis (including differences between Hologic & GE-Lunar)
- Aftercare of patient
- Obtaining an optimum scan
- Follow-up scans and special requirements

Techniques of pDXA

- Patient preparation – prior to scan appointment and at the appointment
- Previous examinations to hand – ensures same scan mode: identifies previous problems
- Peripheral measurements – handedness: non dominant wrist
- Heel measurements – cleaning foot etc.
- Positioning, acquisition and analysis
- Aftercare of patient
- Obtaining an optimum scan
- Follow-up scans and special requirements

Special applications

- Lateral vertebral assessment (LVA)
- Total body
- Challenges of paediatric scanning
- Scanning in young women

Error and artefacts in DXA and pDXA

- The Instrument – calibration, quality assurance
- The Operator – patient positioning, image analysis, operator intervention, intra operator variation
- The Patient – anatomical problems e.g. extra vertebrae, paget's disease, metal artefacts, prostheses etc
- The Report – lack of clarity, misunderstanding the data, relevance of reference data, age, ethnicity

Quality control, quality assurance and radiation protection

- Quality control for DXA scans
- Performance of DXA QC
- Phantoms for DXA QC
- Interpretation of QC plots
- Maintenance, repair and replacement of DXA scanners
- In-vivo precision and its affect on patient follow-up scans
- Procedure for patient follow-up scans
- Radiation dose to patient and operator from DXA scans
- Ionising Radiation (Medical Exposure) Regulations 2000
- Local rules for bone densitometry
- Hazards of ionising radiation
- Radiation hazards to the patient and the operator
- Radiation protection of the patient and the operator
- Difference between accuracy and precision
- Factors affecting accuracy and precision
- Operator and scanner dependent factors affecting QC
- Purpose of instrument QC

NB Please note that delegates will not be examined on mathematical equations or manufacturers' specific information. The examination requires knowledge of general principles rather than details about specific devices.

Radiation Protection (IR(ME)R Syllabus

The use of X-rays in bone densitometry

- The electromagnetic spectrum
- Production of X-rays in a diagnostic X-ray tube
- Spectrum of X-rays from an X-ray tube
- Interaction of X-rays and matter
- Physical principles of DXA
- Production of dual-energy X-rays for DXA
- Fan-beam and pencil-beam DXA
- Table top and peripheral DXA
- Physical principles of pQCT

Radiation hazards and radiation dose

- Biological effects of radiation
- Non-stochastic and stochastic effects
- Ways of measuring radiation dose
- Radiation risk to patients

Statutory requirements and legislation

- Source of legislation and guidance notes
- Health and Safety at Work Act 1974
- Ionising Radiation Regulations 1999
- Framework for radiation safety
- Ionising Radiation (Medical Exposure) Regulations 2000

Radiation protection of patients

- Justification of radiation exposure of the patient
- Dose optimisation – ways to minimise patient dose
- Importance of correct analysis of scan
- Clinical evaluation of outcome
- Patient identification and consent
- Pregnancy and potential pregnancy
- Investigations in children
- Medical and biomedical research
- Health screening
- Medico-legal issues
- Use of previous scans and alternative techniques
- Untoward incidents and notification of faults

Radiation protection of staff

- Principles of radiation protection
- Hazards from primary and scattered radiation
- Dose limits to staff in IRR 1999
- Reduction of exposure to scattered radiation
- Dose rates due to scattered radiation during scanning
- Dose monitoring
- Ionising Radiation Regulations
- Controlled areas and local rules
- Writing local rules for bone densitometry

National Training Scheme
for Bone Densitometry

National Osteoporosis Society

CERTIFICATION ADMISSION APPEAL FORM

Please enclose a copy of your full CV with this form:-

DELEGATE NUMBER: _____

SURNAME (Dr/Mr/Mrs/Ms): _____

FIRST NAME: _____

POSITION: _____

INSTITUTION/COMPANY: _____

_____

ADDRESS: _____

_____

TOWN: _____ POSTCODE: _____

DAYTIME TEL: _____ FAX: _____

EMAIL: _____

EMPLOYMENT DETAILS:-

Sector

- ☐ NHS
- ☐ University
- ☐ Private Health
- ☐ Pharma Company
- ☐ Manufacturer
- ☐ Other (please specify)

Job title

- ☐ Radiographer
- ☐ MTO
- ☐ Clinical Scientist
- ☐ Nurse
- ☐ Medical Doctor
- ☐ Other (please specify)

PTO

SCANNING EXPERIENCE:

	CLINICAL PRACTICE		RESEARCH	
Currently working				
a) DXA / pDXA	☐ hours	☐ days/week	☐ hours	☐ days/week
b) QCT / pQCT	☐ hours	☐ days/week	☐ hours	☐ days/week
c) QUS	☐ hours	☐ days/week	☐ hours	☐ days/week
Previous experience				
a) DXA / pDXA	☐ months full time ☐ months part time*		☐ months full time ☐ months part time*	
b) QCT / pQCT	☐ months full time ☐ months part time*		☐ months full time ☐ months part time*	
c) QUS	☐ months full time ☐ months part time*		☐ months full time ☐ months part time*	

***Part time is defined as 1 or more days per week**

BRIEFLY EXPLAIN WHY YOU FEEL YOU SHOULD BE ACCEPTED TO PROCEED TO CERTIFICATION:

SIGNATURE ..... DATE .....

Please return to Judith Wraight, National Osteoporosis Society, Manor Farm, Skinners Hill, Camerton, Bath, BA2 0PJ, as soon as possible.

National Training Scheme
for Bone Densitometry

National Osteoporosis Society

PORTFOLIO REQUIREMENTS 2009

A. Purpose of the portfolio

The portfolio should contain evidence that demonstrates your understanding and practical ability in bone densitometry such as, quality control, techniques of data acquisition and analysis and the scan print out, providing evidence that shows safe and effective practice.

B. Portfolio submission

Please submit **TWO COPIES** of your finished portfolio, in the blue folders provided, to the National Osteoporosis Society, Camerton, Bath, BA2 0PJ, by **7th October 2009.** We recommend that you send them by recorded delivery. The master copy must include original scans and should be labelled as such. The second copy can include photocopies. It is important that you also keep a third copy for your own records. The National Osteoporosis Society will provide delegates with feedback from the examiners but not return the portfolios.

The majority of candidates who do not pass the portfolio do so because they do not follow the instructions given in this document. Please read carefully.

C. Portfolio compilation and other important information

1. The contents of the portfolio should be included in the order outlined in section D (below) and separated into sections using labelled dividers.

2. The pages of the portfolio should be numbered and a detailed index, with section headings, included. Each case should also be numbered.

3. Scan images should be presented in black and white and in such a way that regions of interest and bone edges are clearly seen. Graphs are acceptable in colour. Photocopies are not acceptable in the master portfolio but can be included in the second copy. Scan images should be of the original area scanned and in the case of GE Lunar scans, magnified if necessary (e.g. the femoral shaft must be clearly seen on a hip scan). GE Lunar users should contact the application specialist for local advice on how to achieve this. Hologic users need to include 2 printouts when excluding a vertebra for technical reasons – one showing all vertebrae and one with vertebra excluded

4. Do not write or type your name on any pages of the portfolio (with the exception of the candidate information sheet and signed declarations) but please include your initials on the scan printouts (as confirmation that you carried out each scan; note, previous scans in a repeat series need not have been carried out by yourself). Please remove/cross out (using a black pen) patient names and patient ID included in the portfolio.

5. All written work should be typed.

6. The portfolio must be **all your own work** and described in **your own words.** Information provided by physicians or manufacturers is not acceptable.

Please note that any communication to the National Osteoporosis Society regarding the training course should be made by email (courses@nos.org.uk) or by post. The committee will respond to queries as quickly as possible.

CONTINUED...

D. Portfolio contents

Each portfolio must contain all of the following in the correct order:

- **Signed Statement by candidate and local supervisor (forms provided)**
- **Candidate Information Sheet (form provided)**
- **Index**

Section 1. QC information on your densitometer

a. A graph of QC BMD data/time over 3 months. QC scans should not pre-date the lecture course The graph may be system generated, plotted in Excel or hand drawn. The graph should be sufficiently clear to see the individual points, variations and trends. Include a paper printout of one of the QC scans of the phantom used to monitor your machine. For GE-Lunar machines use the **aluminium spine phantom.**

b. In approximately 500 words describe the following:-
- how the phantom is scanned and analysed
- comment on the results shown on your graph
- indicate how these results are used to monitor the performance of your densitometer
- With reference to the QC graph you have provided, comment on the mean, Standard Deviation, trends over time and any sudden changes.

c. This information need only be supplied for one scanner.

Section 2. Scans:

a) Describe in your own words the standard procedure i.e. positioning and analysis of scans used in your department for each anatomical site used in this section (approximately 500 words per site).

b) Include:
20 cases, each with scans from two anatomical sites (e.g. spine and hip, spine and forearm, spine and heel, spine and total body, hip and forearm, hip and heel)

or

40 single-site cases

All scans must have been performed and analysed by yourself

Images acquired for vertebral assessment may be included if they help to clarify spinal problems, but will not count as one of the two anatomical sites.

Scans must not pre-date the lecture course. Include as wide a variety as possible to demonstrate some of the clinical and technical issues that are encountered in your work e.g. degenerative disease, scoliosis, or metal artefacts. Where follow-up cases are presented, provide a copy of the previous scans and the trend graphs, even though another operator may have performed this. Lunar users must include the ancillary print out sheet (height/width of vertebrae of the spine).

For each case supply the following:

- A complete set of printouts for each scan (noting the instruction in paragraph C.3), with one image per printout. Composite printouts that show both the spine and hip on a single page are not acceptable.

- On a separate sheet of paper:

- reason for referral
- brief discussion of any difficulties with patient positioning, scanning, choice of scan mode and analysis of the data, with reference to any deviations from the norm
- brief comment on any aspects of the process or result which might render its normal interpretation unreliable.

If scans are obtained from more than one machine please ensure they are from the same manufacturer

CONTINUED...

Section 3. **A copy of the scan print out** for one anatomical site from your equipment on a chosen patient including scan image, reference graph, normative data. You should comment on the relevance of the information and explain how it helps with determining the reliability of the result or the status of the patient's bone strength.

Explain (**DO NOT** simply list) **ALL** the information on the print out including:-

- patient demographics
- scan demographics
- image
- results
- graph
- scan parameters
- T-scores
- Z-scores
- % of normal
- choice of reference population data and reasons for choice

Your print out should include all of the above, if not, please ensure that an explanation is given.

Section 4. **Three contrasting case studies** with a description for each study including:

a. Reason for referral and brief clinical history
b. Description of technique (scan and analysis) and explanation of scan sites and modes used
c. Discussion of any problems with patient positioning
d. Discussion of any difficulties with scan acquisition
e. Description of scan analysis and result
f. Brief summary of clinical outcome i.e. the effect of scan on patient management
g. At least one case study should be a follow-up study with print outs, trend graphs and analysis (please include previous print outs for all follow-up studies included in this section)

Please include all scan printouts including any previous scans, even though another operator may have performed the scans.

E. Portfolio Marking

The portfolio will be marked on the following criteria:

Quality Control

1. Adequate number of points on the QC plots
2. Details of technique (scan and analysis)
3. Comments on measured mean compared to manufacturer's stated value
4. Comments on the use of data to monitor the performance of your particular machine (even if no problems arise)

Scans

1. Correct number and adequate range of scans
2. Details of reason for referral
3. Correct positioning of patient and comment on any problems encountered
4. Comments on scan parameters
5. Correct analysis and comment on any problems encountered
6. Comment on artefacts or unusual features

CONTINUED...

Scan Information Analysis

1. Image, scan information, results and graph printouts included
2. Satisfactory comment on all demographic, image, graphical and technical data given in report
3. Level of understanding of BMD result, T-scores, Z-scores, % of normal and reference data used

Case Studies

1. Reason for referral and brief clinical history
2. Description of technique (scan and analysis) and explanation of scan sites and modes used
3. Discussion of any problems with patient positioning
4. Discussion of any difficulties with scan acquisition
5. Description of scan analysis and result
6. Summary of clinical outcome

National Training Scheme for Bone Densitometry

Pre-Course Recommended Reading

If you are interested in undertaking some reading in the areas of osteoporosis and bone densitometry before starting the course, the following selection of reference materials are recommended:

National Osteoporosis Society

The National Osteoporosis Society website www.nos.org.uk contains useful information about osteoporosis. Of particular interest will be the Position Statements and Guidelines on bone densitometry (http://www.nos.org.uk/NetCommunity/Page.aspx?pid=2998srcid=240). (Please note, copies are sent to all new Professional Members of the National Osteoporosis Society).

Other reading

1. Nigel K Arden. Osteoporosis. Publisher: Remedica. ISBN: 1-850092-05-2
2. Glen M Blake, Heinz W Wahner & Ignac Fogelman. The Evaluation of Osteoporosis: Dual Energy X-ray Absorptiometry in Clinical Practice. Publisher: Taylor & Francis. ISBN: 1-85317-472-6
3. Sydney Lou Bonnick & Lori Ann Lewis. Bone Densitometry for Technologists. Publisher: Humana Press. ISBN: 1-58829-020-4
4. Sydney Lou Bonnick. Bone Densitometry in Clinical Practice – Application and Interpretation, Second Ed. Publisher: Humana Press. 2004.
5. Cummings, S. R. and Melton III, L. J. Osteoporosis I: Epidemiology and outcomes of osteoporotic factures. Lancet 2002;359:1761-1767.
6. Delmas, P. D. Osteoporosis IV: Treatment of postmenopausal osteoporosis. Lancet 2002:359:2018-2026.
7. Fordham, J. N. Manual of Bone Densitometry Measurements: An Aid to the Interpretation of Bone Densitometry Measurements in a Clinical Setting. Publisher: Springer. 2000.
8. HK Genant, G Guglielmi & M Jergas. Bone Densitometry & Osteoporosis. Publisher: Springer. 1998.
9. Graham D.T. and Cloke P. Principles of Radiological Physics (2003; 4th edition). Churchill Livingstone. ISBN: 0-443-07073-3.
10. Kanis, J. A. Osteoporosis III: Diagnosis of Osteoporosis and Assessment of Fracture Risk. Lancet 2002; 359:1929-1936.
11. Paggiosi, M. Quantitative Ultrasound for the Assessment of Bone Status. Synergy. 2002; 33:22-28.
12. Royal College of Physicians. Osteoporosis: clinical guidelines for prevention and treatment. London, England: Royal College of Physicians, 1999. www.rcplondon.ac.uk/
13. Royal College of Physicians and Bone and Tooth Society of Great Britain. Osteoporosis: clinical guidelines for prevention and treatment. Update on pharmacological interventions and an algorithm for management. London, England: Royal College of Physicians, 2000. www.rcplondon.ac.uk/
14. Seeman, E. Osteoporosis II: Pathogenesis of bone fragility in women and men. Lancet 2002;359:1841-1850.
15. Anne Sutcliffe. Osteoporosis – A Guide for Healthcare Professionals. Publisher: Whurr. 2006
16. Journal of Clinical Densitometry, Volume 11 No 1. This contains the latest International Society for Clinical Densitometry (ISCD) position statements and background papers on their derivation. Please note that where there is a conflict, UK guidance should be adhered to.

Further recommendations

1) It may be helpful to familiarise yourself with the work being done on clinical standards in your country: NICE (England and Wales) / SIGN (Scotland) / GAIN (Northern Ireland).

2) International Osteoporosis Foundation (IOF) Vertebral Fracture Initiative http://www.iofbonehealth.org/health-professionals/educational-tools-and-slide-kits/vertebral-fracture-teaching-program.html

3) To review any training you have already received including information from the manufacturers.

National Training Scheme
for Bone Densitometry

National Osteoporosis Society

APPLICATION FORM FOR CERTIFICATION

Candidate Information

NAME..... (Dr/Mr/Mrs/Ms) CANDIDATE NUMER .....

POSITION..... INSTITUTION/COMPANY.....

ADDRESS .....TOWN.....

POSTCODE..... DAY TIME TEL ..... FAX .....

EMAIL .....

Local Supervisor Information

NAME..... POSITION.....

DAYTIME TEL..... EMAIL.....

PLEASE CIRCLE AS APPROPRIATE

- I HAVE/HAVE NOT READ THE RULES & REGULATIONS
- I HAVE/HAVE NOT READ THE PORTFOLIO REQUIREMENTS DOCUMENT
- I HAVE/HAVE NOT RECEIVED TRAINING IN ONE OR MORE TECHNIQUES OF BONE DENSITOMETRY
- I AM/AM NOT CURRENTLY EMPLOYED IN CLINICAL PRACTICE
- I WILL/WILL NOT HAVE SIX MONTHS FULL TIME OR 12 MONTHS PART TIME (1 DAY/WEEK OR MORE SCANNING EXPERIENCE BY 16th March 2009)

PLEASE TICK AS APPROPRIATE

I have attended the following modules of the lecture courses:

CORE ☐ DXA/pDXA ☐

I have completed the following IR(ME)R training:

NOS IR(ME)R COURSE ☐ I am a registered Radiographer ☐ Other Radiation Course ☐ (attach details)

I enclose the following documents in support of my application: (NB: Your application cannot be processed unless these documents are enclosed)

A copy of my registration certificate ☐
or
A copy of my professional qualifications ☐
plus
A letter from my current employer confirming my position ☐
plus
My course passport ☐

EXAMINATION REGISTRATION

The on-line examination is on Tuesday 7th July 2009

I would like to register for the examination of the Core module and DXA/pDXA Module ☐

I would like to sit the exam at the following centre:

Glamorgan ☐ **Leeds** ☐ **London** ☐ **Dublin*** ☐ **Edinburgh** ☐

***This centre will only be offered if there is sufficient interest**

My second choice is.....

I am unavailable to sit the exam in July 2009 and would like to sit it in London on Tuesday 8th September 2009 (please provide explanation)

.....

.....

PORTFOLIO REGISTRATION (Portfolio Submission date – Wednesday 7th October 2009)

CANDIDATE SIGNATURE..... **DATE** .....

LOCAL SUPERVISOR SIGNATURE ..... **DATE** .....

FEES (the reduced rate is available to all NOS professional members, NHS employees, university employees and students)

	Standard	Reduced	
Examination:	£170	£130	
Examination Re-sit fee:	£70	£70	
Per Portfolio:	£75	£75	All prices are inclusive of VAT

I enclose a cheque (payable to: National Osteoporosis Society) for a total of £.....

Please debit my Visa/Mastercard £ _ _ _ _ _ _ _ _ _ _

VISA/MASTERCARD NUMBER _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _ ISSUE NUMBER _ _ _ _

VALID FROM _ _ _ _ _ _ EXPIRY DATE _ _ _ _ _ _ THREE DIGIT SECURITY NUMBER _ _ _ _

Signature of card holder ..... Date.....

Return to:

Judith Wraight
National Osteoporosis Society
Camerton
Bath
BA2 0PJ

No later than Friday 17th April 2009.

National Training Scheme *for* Bone Densitometry

Instructions for Portfolio Marking (2007/8 Round)

1) Fill in the Student Number, Initials of Examiner, Date, Technique and Machine Type on the Portfolio Score Sheet.

2) Question Scoring

Using the scoring criteria below , insert your mark for each component within a section on the Portfolio Score Sheet. At the end of each section add up the total score.

Scoring criteria

a) Yes/No questions:

In most cases, Yes scores 2 and No scores 0. If there is some doubt over whether requirement has been fully met, a mark of 1 may be allocated.

b) Qualitative questions

In general:

	Mark
Not acceptable or not attempted	0
Attempt made but does not fully meet requirement or does not appear to fully understand	1
Acceptable, meets requirements and demonstrates good understanding	2
Provides a full comprehensive response demonstrating thorough understanding. More than expected.	3

NB please refer to Portfolio Requirements Form given to candidates and the comments on the attached Portfolio Score Sheet

3) Score Summary

Fill in the score summary table on the final page of the Portfolio Score Sheet. For each section please include the section score and whether you consider the section to be a pass or fail. Please give the total score for the portfolio and state if you consider the portfolio as a whole to be a pass or fail. NB All four sections must be passed for an overall pass to be awarded.

Portfolio sections pass marks 2007/8

Section 1	*15*	*out of total possible of*	*22*
Section 2	12	""	17
Section 3	*15*	""	*30*
Section 4	*19*	""	*37*

All fails will be sent for second marking.

4) Sign, Print your Name and date the Score Sheet.

5) Portfolio Feedback Form

Fill in the candidate's ID number on the sheet. Please provide detailed constructive comment on the portfolio especially highlighting areas where improvement is required. The information on this form should be typed. This feedback will be passed back to the candidate regardless of pass/fail status.

Overview of the Bone Densitometry Service

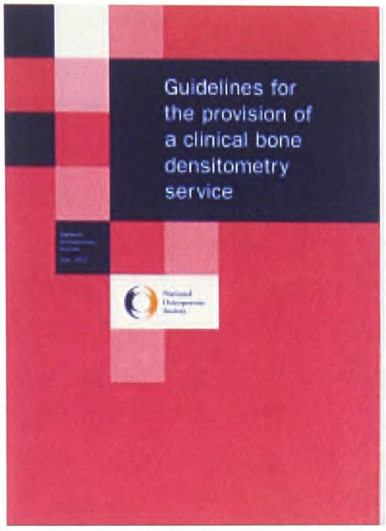
Ms. Sue Steel,
Consultant Physicist,
Hull & East Yorkshire
Hospitals Trust

National Osteoporosis Society

NOS standards for a hospital based densitometry service

- Procedures and organisation
- Protocols and equipment
- Staffing

National Osteoporosis Society



National Osteoporosis Society

Procedures and organisation 1

- Written guidelines for referral
  - Agreed with commissioners and users
- Written request
- Authorisation of request
- Appointment letter
- Questionnaire
- Appointment diary

National Osteoporosis Society

Procedures and organisation 2

- Reception & waiting area
- Provision for patient privacy and dignity
- Information should be available on:
    - Osteoporosis and support groups
- Patient advised to contact referring doctor for result
- Scan to be reported by experienced medical practitioner
- Clinic referral available if required

National Osteoporosis Society

Protocols and equipment 1

Written procedures required on:

- All aspects of service
- Women of childbearing age
- Quality control

National Osteoporosis Society

Protocols and equipment 2

- Database/audit
- Trained operators
- Archive & backup
- Maintenance records
- Equipment safety
- Choice & commissioning

National Osteoporosis Society

Staffing 1

- Operators
  - Trained
  - CPD
- Scientific support
  - Supervision & analysis of QC data
  - Troubleshooting
  - Training

National Osteoporosis Society

Staffing 2

Medical Practitioner should:

- Be clinically responsible for service
- Be responsible for validation of requests (protocols)
- Define scan protocols (sites)

National Osteoporosis Society

Staffing 3

Medical Practitioner should:

- Be familiar with principles of DXA including precision, anomalies, artefacts
- Report scans – be familiar with clinical utility of DXA and relevance of WHO definition, T & Z-scores, significant change
- Participate in relevant CME

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Staffing 4

- Clerical/secretarial:
  - Appointments
  - Typing reports
- Receptionist
- Nursing support

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Staffing 5

RPA:

- Approval of premises and procedures
- Ensure adherence to local rules

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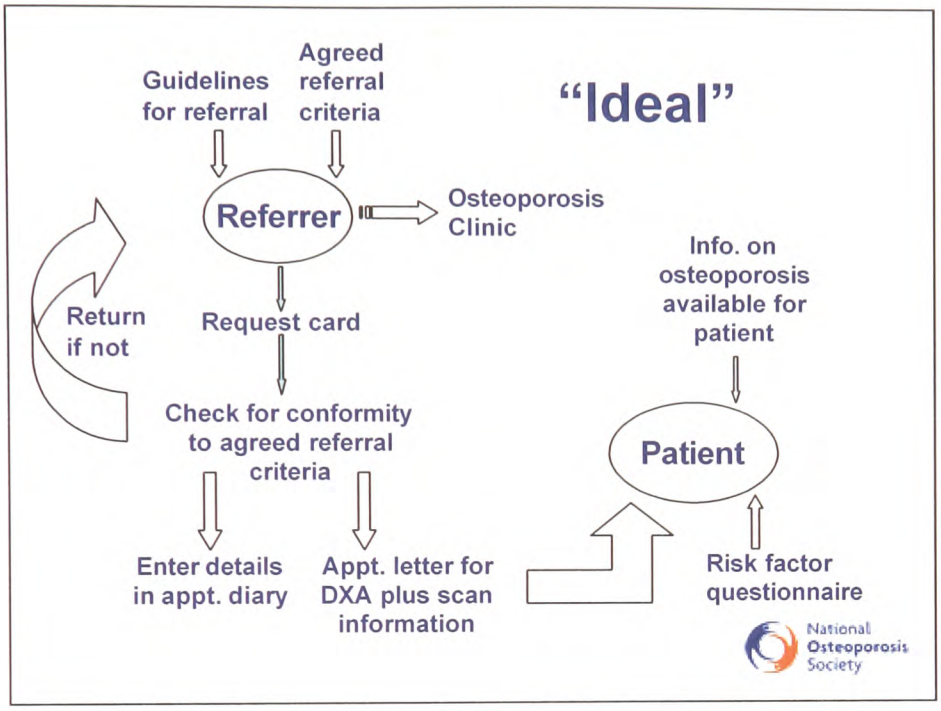
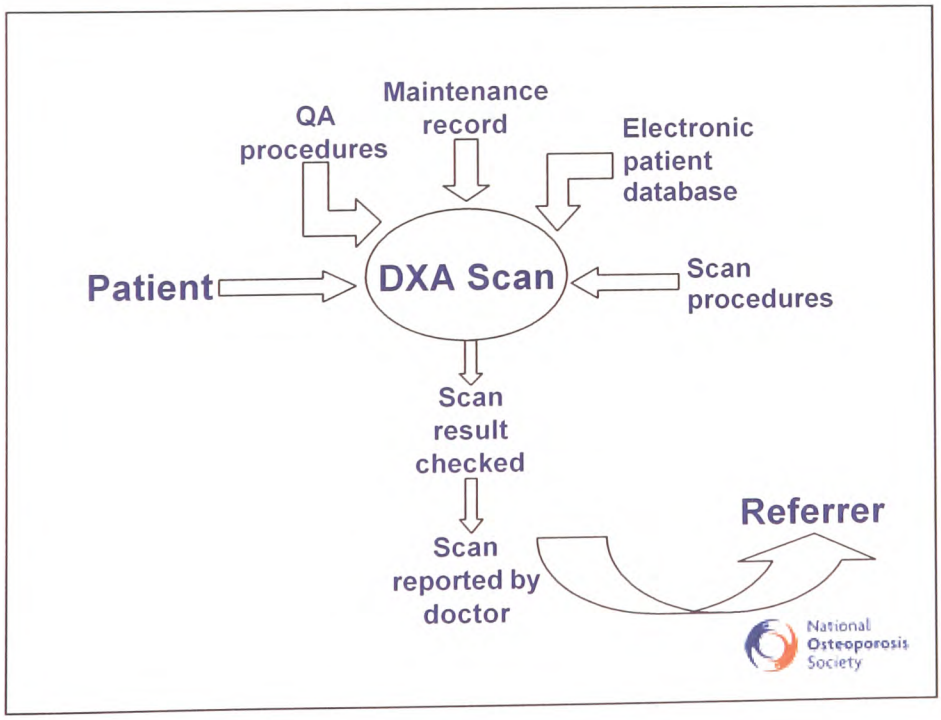

"Ideal"
Guidelines for referral
Agreed referral criteria
Referrer
Osteoporosis Clinic
Return if not
Request card
Check for conformity to agreed referral criteria
Enter details in appt. diary
Appt. letter for DXA plus scan information
Info. on osteoporosis available for patient
Patient
Risk factor questionnaire
National Osteoporosis Society


QA procedures
Maintenance record
Electronic patient database
Patient
DXA Scan
Scan procedures
Scan result checked
Scan reported by doctor
Referrer
National Osteoporosis Society

Principles of Dual Energy X-Ray Aborptiometry (DXA)

Ms. Sue Steel,
Consultant Physicist,
Hull & East Yorkshire Hospitals Trust

National Osteoporosis Society

Dual energy X-ray absorptiometry (DXA)

- Two different energy X-rays
- Absorbed by the body to varying degrees dependent upon characteristics of the X-rays and the tissues

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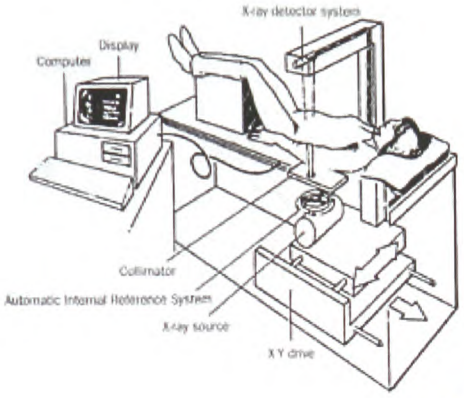
Principle components of a DXA System



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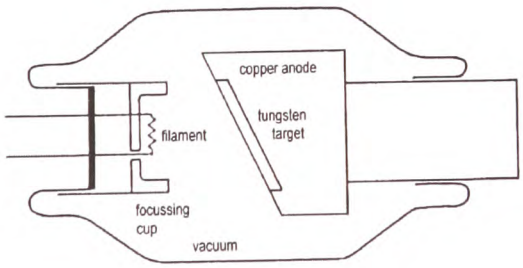
X-ray tube

An X-ray tube is a vacuum tube in which X-rays are produced when a beam of high speed electrons strikes a metal target



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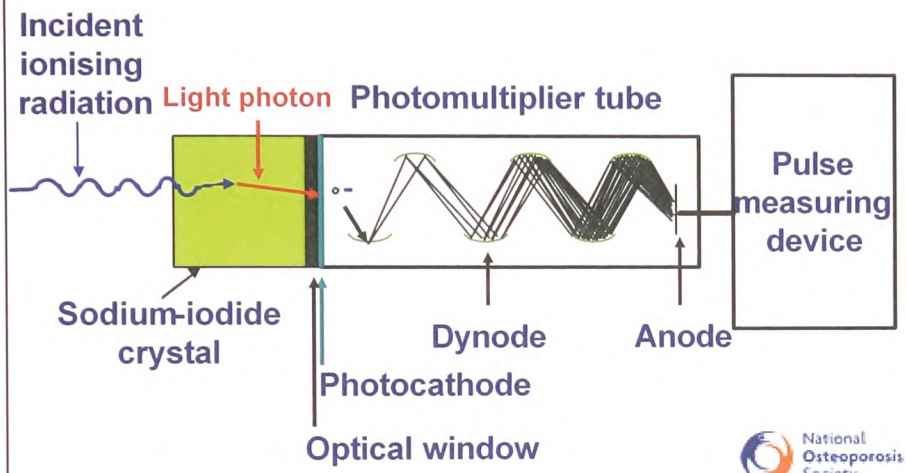
Scintillation detectors



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Environmental considerations

- Stable power supply
- Temperature
- Humidity
- Vibration

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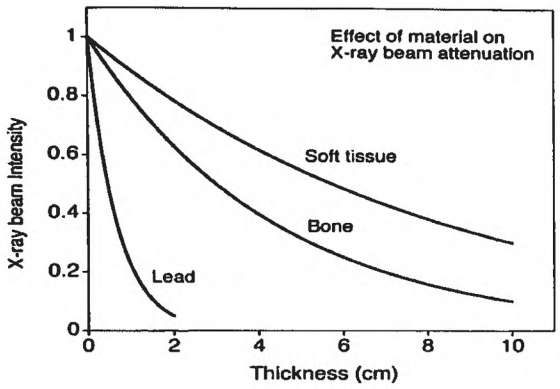
Transmission of X-rays



The transmission of X-rays depends on the material they are passing through.....

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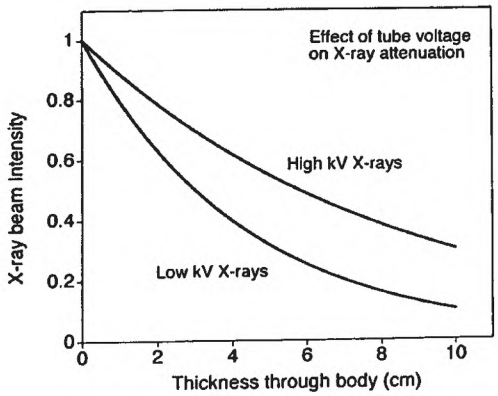
Transmission of X-rays



..... and their photon energy

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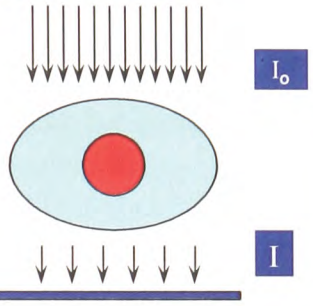
X-ray interactions

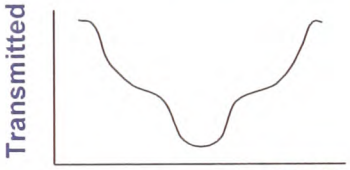
- Incident beam (I_o)
  - X-rays which enter
- Transmitted beam (I)
  - X-rays which exit
- Attenuation
  - $I_o - I$



$$I = I_o e^{-\mu x}$$

x = thickness of material

μ = linear attenuation coefficient



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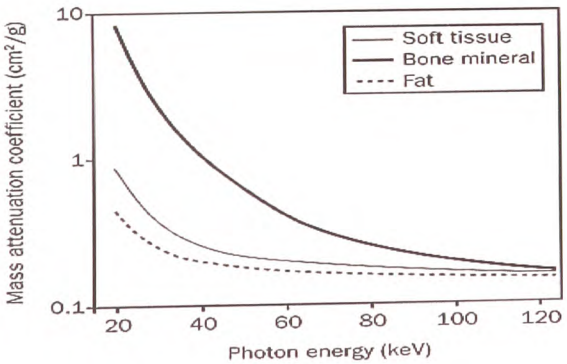
Variation of mass attenuation coefficient for bone and soft tissue with photon energy



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Why dual energies?

- Differential absorption by bone and soft tissue
- 30-50 keV
  - Bone mineral attenuation >> soft tissue
- >70 keV
  - Bone mineral attenuation approximates soft tissue

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Why dual energies?

- Two simultaneous equations quantify:
  - Attenuation due to bone
  - Attenuation due to soft tissue
- Calibrated to give BMD (gcm^{-2}) using known bone and tissue standards:
  - In calibration block (Lunar)
  - Internal calibration filters (Hologic)

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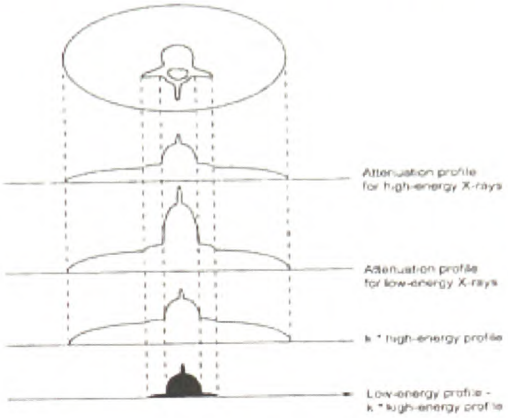
DXA attenuation profiles

$$A_{Bone} = A_{Low} - K\,(A_{High})$$



Factor K = ratio of ST attenuation coefficients for low and high energies

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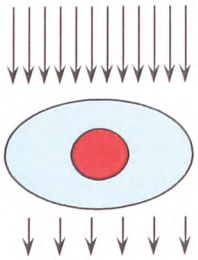
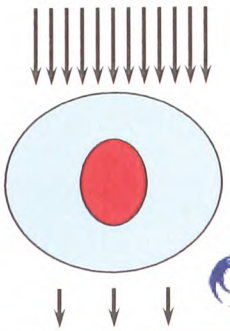
Effect of body size

X-rays of all energies are increasingly attenuated on passing through tissue.

Thin subjects:
- Many X-rays reach detector
- Good counting statistics (if detector can cope!)



Obese subjects:
- Few X-rays reach detector
- Selective attenuation of low energy X-rays (beam hardening)



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DXA scan modes

Alternative scan modes provided that:

- **Decrease number of X-ray photons for thin subjects (decrease X-ray tube current *and/or* increase scan speed)**
- **Increase number of photons for obese subjects (increase current *and/or* decrease scan speed)**

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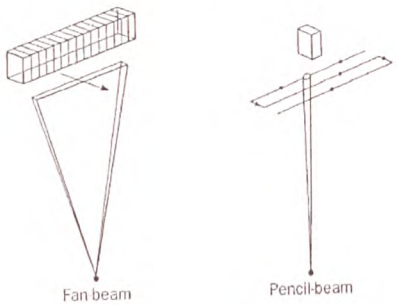
Shape of X-ray beams in DXA



Since the introduction of DXA the most important advance has been the replacement of pencil-beam scanners by fan-beam ones

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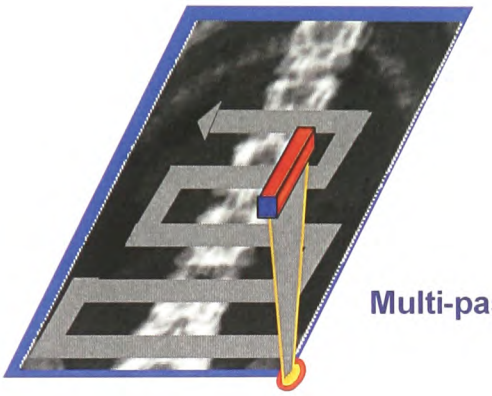
Narrow-angle fan beam



Multi-pass fan beam

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Differences between pencil and fan-beam DXA systems

Pencil-beam DXA	Fan-beam DXA
• Older technology	• Later technology
• Scan time 5-10 min	• Scan time 10-30 sec
• Good image quality	• Better image quality
• Low patient dose (~1 μSv)	• Low patient dose (~10 μSv)

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PIXI

DXL Calscan

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Differences between table-top DXA and peripheral DXA

Table-top DXA

- Used for scanning spine and femur
- X-ray tube voltage ~ 80-140 kVp
- Low patient dose (~10 mSv)

Peripheral DXA

- Used for scanning forearm and heel
- X-ray tube voltage ~ 40-60 kVp
- Very low patient dose (~ 0.1 mSv)
- Portable
- Lower cost

National Osteoporosis Society

The Bone Densitometry Service

The fundamentals of a good clinical bone densitometry service are appropriately trained and experienced staff, reliable equipment, rigorous quality assurance, evidence based referrals and good communication between users, providers and patients.

Overview

A bone densitometry service may take the form of a diagnostic only service within a radiography or other appropriate hospital department. Results may be issued with perhaps only a technical comment on difficulties with patient positioning or scan analysis. This relies on the physicians referring into the service having sufficient training and experience in the limitations and potential inaccuracies of the technique to interpret the results appropriately. Access to such a service is therefore best restricted to specialist clinicians with referrals through a specialist clinic.

Preferably, a bone densitometry service should have the support of a medical practitioner proficient in the field of diagnosis, prevention and treatment of osteoporosis[1]. Comprehensive clinical reports may then be issued providing an interpretation of the bone densitometry results and giving recommendations on patient management[2].

Diagnosis is generally based on the use of dual energy x-ray absorptiometry of the spine and hip and as such is subject to the Ionising Radiation Regulations requiring therefore support and approval of the local Radiation Protection Advisor[3].

Standard operating procedures should be in place for all aspects of the service from receipt of requests to issuing of reports.

Scan requests

The operator should only accept scan requests which are properly authorised according to an established protocol. The request should be formally documented by an approved referral source and should contain sufficient clinical information to justify the examination. As ionising radiation is being used, an approved referral source will be a registered medical practitioner who has received adequate training in accordance with the Ionising Radiation (Medical Exposure) Regulations 2000[4]. Usually a consultant who has this training agrees to be responsible for referrals from GPs under the agreed protocol. The prime considerations are that referrals comply with evidence based agreed referral criteria and that the results of the scan will influence subsequent medical management of the patient.

The standard protocol for referral will contain a list of clinical parameters within which a scan request may be indicated. Evidence based criteria for referral are available[5] and may be adapted locally dependent upon resources available.

Standard criteria for bone densitometry generally include:

- Previous osteoporosis-related fracture
- Radiological osteopenia
- Corticosteroid use
- Diseases associated with osteoporosis such as thyrotoxicosis, RA, malabsorption
- Untreated oestrogen deficiency such as following an early menopause
- Family history

There may also be a requirement for repeat measurements for monitoring of disease progression or treatment effectiveness.

Information for Patients

A written appointment letter should be sent to the patient giving directions to the department, the nature and the purpose of the test, information on suitable clothing and contact numbers if they have any queries or wish to change the appointment. It is helpful to enclose an information leaflet on precisely what the test involves which includes pictures to help reassure the nervous patient. An Osteoporosis risk factor questionnaire may be completed when the patient attends or could be sent out with the appointment letter. Information provided on prior fracture or hip replacement helps the operator avoid unnecessary discomfort when positioning the patient and unnecessary radiation exposure. Details of relevant medical and lifestyle factors can aid the reporting clinician provide an individualised advice.

A diary of appointments should be kept and a policy established for non attendees.

Patient Handling

If the patient has been scanned previously at the same unit every effort should be made for the scan to be carried out on the same machine as on previous occasions in order to maximise reproducibility.

On attendance the patient should be welcomed and any concerns regarding the scan addressed. As for all diagnostic procedures, the operator should ensure that they have the correct person as indicated on the request card/letter before proceeding with the test. The patient should be called by their first name and surname and prior to scanning asked to provide their date of birth and home address. This data should be checked against the request card in order to reduce the possibility of scanning the wrong patient.

Women of child bearing age should be asked to confirm that they do not believe themselves to be pregnant. How this information is recorded depends on the protocol of the institution concerned.

The operator should confirm that there are no metal objects or bulky clothing within the area to be scanned. Changing facilities should be available for patients to change into a gown if necessary.

The patient should be informed that a small amount of ionising radiation is being used. It is useful to place this in perspective by comparing it to naturally occurring background radiation.

Implicit informed consent is assumed by virtue of the fact that the patient attends for a scan, the reason and nature of which has been explained to them. However consent may be withdrawn at any time and the operator should comply and report this to the referring clinician[6,7]. Children of sound mind between the ages of 16 and 18 are assumed to be capable of giving or refusing consent. Scans of younger children are generally carried out only in centres specialising in paediatric bone disease and for these consent of a parent or guardian may be requested[8,9]. The operator does have a responsibility to help and encourage all patients to comply with the request for a scan but without coercion.

Privacy and dignity should be preserved throughout the scanning procedure. On

completion, the operator should tell the patient how and when they will be informed of the results of the scan.

Confidentiality

Any information obtained from a patient in the course of attendance for a scan is strictly Confidential. The operator may discuss information with the patient which has been obtained as a result of the scanning procedure, provided that this is in line with an agreed protocol developed within the employing authority. The patient has a legal right to see any personal information being held by the health authority and the health authority has rights of access to the patient's health records [10,11,12,13,14].

Quality Assurance

Equipment should be regularly maintained and service and repair records kept. It is helpful to keep a log of any relevant daily observations. A rigorous quality assurance programme should be followed and results carefully monitored. Scientific support should be available for supervision and analysis of the quality control data and for trouble shooting of faults with the equipment.

Scans should be performed and analyzed by trained operators following standardized protocols. It is best having dedicated operators performing this type of work to optimize results. Operators should be trained health care professionals who must maintain their skills and knowledge through continued professional development. They should also undergo radiation protection training and have knowledge of the background of Osteoporosis.

Reporting

Reporting of bone density results may be based on the WHO criteria but these are applicable to post menopausal females only[15]. The image should be checked for correct poisoning, analysis, artefacts and general technical accuracy. When monitoring changes over time positioning, analysis and software versions should be considered. A knowledge of measurement error is required to determine whether any change is significant[16]

Results should be interpreted in conjunction with patient specific risk factors such as prior fracture, age and steroid use.

Audit

A database of referrals should be maintained to aid clinical audit and help in identifying previous patient attendance.

Information on Bone Densitometry and Osteoporosis

The National Osteoporosis Society (NOS) is a good source of information for patients and has prepared a free information sheet on bone density measurement which answers common concerns raised by patients.

Leaflets and booklets are also available from the NOS for healthcare professionals.

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Data Management and Report Generation

Data Management and Report Generation

Introduction

Bone densitometry investigations generally involve computer controlled acquisition, processing and analysis of data. The increasing prevalence of osteoporosis heightens the need to identify those at risk and can produce an unexpectedly high demand on a newly introduced densitometry service. This in turn will entail the accrual of copious amounts of data that require a comprehensive database structure together with careful storage and backup procedures in order to maintain data integrity. The rigorous quality assurance procedures that should be implemented to monitor and ensure accuracy and precision of the results, add to this burden of data management.

Data Management

Most commercially available bone densitometry systems provide software tools for the maintenance of both patient and quality assurance data. However, the user needs to be aware of the extent and limitations of these tools and how best to employ them to assist with the management of their routine referrals and clinical trials. In units with only one densitometer, the software provided may suffice. However, in larger centres a more comprehensive and automated system is highly desirable.

All computer based clinical systems must provide a file structure, or database, such that the record of one patient cannot be mistakenly associated with another. This is an essential criterion when considering the purchase of equipment. Data integrity is generally achieved with the aid of a unique identifier, a code that is unique to each patient, which is allocated by the system and is an integral part of the file containing the patient's biographic
information. If the scan or investigation results are subsequently stored in separate files, as in a relational database, this unique identifier is also incorporated in those files in order to provide a cross reference. Alternatively the biographic file may contain a separate field which indicates the name of the file in which relevant results are located.

Some computer based systems, such as those supplied by GE-Lunar (GE-Lunar, Madison, WI) provide facilities for grouping patient files into separate directories (computer filing systems) which is useful where several research studies and clinical referrals may be conducted on a single machine. Participation in clinical drug trials normally requires the setting up of a separate file system for each trial.

Properly organised and separated data files provide ease of access for each particular study but have the disadvantage of the need to search several directories to determine previous attendance when given only the patient's name. Other systems, such as Hologic (Hologic Inc., Waltham MA) store all patient files in one directory but provide user defined search routines that enable patients attending for particular studies to be easily identified. This
method relies on an initial entry of a unique code related to each study in one of the fields provided. It is well worth taking time when setting up a densitometry service to ensure, as far as possible, that the database is structured to address future requirements.

A densitometry centre fortunate to have more than one system for determining bone density also needs to take steps to ensure that a patient's previous visits can readily be identified so that follow up studies can be carried out on the same machine. This is crucial even where the machines are of the same type from the same manufacturer as inter machine differences may exceed the minor changes that occur in bone density, whether as a result of age or menopause related loss or treatment gain[1]. The methods for achieving ease of patient identification where multiple databases exist include a card index system and a separate patient administration computer database.

The first is slow but useful where requests are received on cards although cards would

need to be made out for those attending for research or clinical trials. Additional details regarding the relevant densitometry system and database would need to be manually entered and, if easy access to results is required, the densitometry results would also need to be included. Manual entry is tedious and a potential source of human error.

The second requires manual entry onto a computer of relevant machine, database and patient details and, if required, densitometry results. This is again prone to human error and entails a time consuming duplicate entry of patient details. A preferred method would provide for amalgamation of the densitometry databases into one patient administration database.

Transfer of Quality assurance data from the densitometer facilitates monitoring of equipment performance parameters using more sophisticated analysis tools such as Microsoft Excel or SPSS. In some densitometry centres, additional data is collected from the patient on clinical, social and lifestyle factors thought to influence bone density and osteoporosis risk. If these details are entered into an electronic database they may be merged with the bone densitometry results and used for automated generation of more individualised reports.

Thought should be given to database management at the outset, with due consideration for future potential development, as restructuring a poorly designed set up can prove difficult and expensive.

Careful attention should also be paid to the establishment of data backup and archive procedures to ensure space availability on the computer system and security of patient data. Computers are currently a prime target for opportunist thieves. Assuming the computer is physically secure, it is still prone to software or hardware failure that may incur loss of data. Software should be available on the system to enable novice users to achieve copying of data to an appropriate backup media. Consideration should be given to the amount of computer memory required for the storage of image files when choosing the backup media. The manufacturers provide recommendations on backup and archive intervals but individual centres should determine their optimum routine based on workload and quantity of data at risk. It should also be noted that the backup media is not foolproof and it is recommended to keep more than one copy in separate locations. These copies may be in the form of daily archive disks of patient investigation results and weekly, more comprehensive, backup discs. It is recommended that the backup disc be stored in a secure location in a separate room.

Any person responsible for the management of databases containing personal details on individuals must be fully informed of the need to ensure confidentiality and safety of that data. This is especially important where sensitive medical details are concerned. The Data Protection Act of 1984 requires registration of databases and system managers. Larger healthcare providers should have a data protection officer who will be able to advise on
such matters. Due consideration should also be given to confidentiality when disposing of computers on which patient details have been held.

Report Generation

In order that bone densitometry assessment may assist in the clinical management of the patient, a meaningful report must be supplied that is understandable to the referring physician[2]. Referrals for densitometry may be received from several sources dependent upon the specific contract agreements for each densitometry centre. The service may provide for a report of the measurement only or, preferably, for result interpretation and patient management guidance.

A technical assessment of the results, including osteoporosis status and possibly fracture risk assessment based on patient's results and age, may be given. This would require a reasonable understanding by the referring practitioner of bone densitometry, osteoporosis risk assessment and management. Where individualised reports are produced by an experienced physician, providing a clinical summary and management advice, specialist knowledge is made available to the referring practitioner. Ideally, the process should be automated.

Where a technical report is to be provided, only limited clinical details are required in order to ensure the appropriateness of the request and aid in the interpretation of the results. The printing of appropriate criteria for referral on a densitometry request card, to be checked off by the referring clinician, may aid in reducing inappropriate referrals. Factors influencing the densitometry procedure, such as hip replacements, laminectomy or radiologically diagnosed vertebral fracture, should be included on the request card as patient obtained history may prove unreliable. When a more comprehensive report and guidance is to be given, full details of the patient's relevant history need to be obtained.

Generally, the referring physician, especially if a GP, requires to know "Do they have the disease?", "Are they likely to develop the disease?", "Do they require treatment and if so for how long?". The scan printout generated by the densitometry system software may prove over elaborate and unhelpful. Often, especially with DXA, results are expressed in several forms : actual density (g/cm2), relative to young normal (T score), relative to age matched (Z score), as a percentage of either young or age matched (% young normal/age matched). The World Health Organisation[3] define osteoporosis in postmenopausal women as a bone mineral density value of the spine, hip or forearm of more than 2.5 SD below young normal mean. The T score therefore tends to be used for the diagnosis of the disease whereas the Z score or age matched comparison may be of use in decisions regarding treatment, especially in the elderly[4]. It is helpful for the GP to be provided with an interpretation of the results and recommendation on patient management.

Investigations not resulting in a prompt, clear, concise, clinically useful report will soon fall into disrepute in this age of limited resources and rising demand on healthcare services.

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Position statement on the reporting of dual energy x-ray absorptiometry (DXA) bone mineral density scans

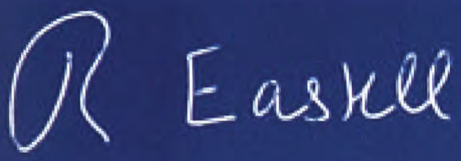
National Osteoporosis Society

June 2002

National Osteoporosis Society

Foreword

This document provides clear guidance to physicians providing a DXA scanning service on how spine and femur bone mineral density scans may be reported to GPs and other referring physicians. Its use will facilitate improved communication between primary and secondary care and may help to alleviate confusion for the patient.



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Position statement on the reporting of dual energy x-ray absorptiometry (DXA) bone mineral density scans

DXA scanning of the axial skeleton is the accepted technique for the diagnosis of osteoporosis. The following statement has been prepared to outline the current advice from the National Osteoporosis Society (NOS) on the interpretation of DXA scans on patients referred by registered medical practitioners.

This position statement applies to DXA scans of the proximal femur and PA lumbar spine only and is based on relevant scientific literature in peer-reviewed journals as of September 2001. It will be reviewed on a biannual basis or as required in the light of new research findings.

This statement was prepared for the NOS by Professor I Fogelman, Professor J Adams, Dr J McCrea, Ms SA Steel and Dr GM Blake and represents the consensus view of the members of the Bone Densitometry Forum Committee. The statement is endorsed by the NOS Council of Management.

June 2002

Key recommendations

1 Bone mineral density (BMD) measurements by DXA at the lumbar spine and proximal femur remain the current 'gold standard' for the diagnosis of osteoporosis and intervention with treatment.

2 This report aims to give guidance to physicians providing a DXA scanning service on how spine and femur BMD scans may be reported to primary care doctors and other physicians referring patients for bone densitometry studies.

3 The basis of the recommended reporting system is the World Health Organization (WHO) study group definitions of osteoporosis, osteopenia and normal, based on BMD T-scores $\leq$ -2.5, between -2.5 and -1, and $\geq$ -1 which identify patients with high, intermediate and low risk of fracture respectively.

4 The WHO definitions of osteoporosis, osteopenia and normal, apply only to BMD measurements of the spine, proximal femur or forearm and should not be applied to other DXA measurement sites or measurements made with technologies other than DXA.

5 Although the clinical diagnosis of osteoporosis is based on T-scores, Z-scores can be helpful in scan interpretation, especially in the elderly.

6 Care is necessary when using reference ranges for the calculation of T-scores and Z-scores that the data used are relevant and accurate for the population concerned taking into account the gender and ethnic origin of the patient. It is recommended that femur BMD measurements are interpreted using the total hip region of interest with the reference range derived from the third US National Health and Nutritional Examination Survey (NHANES III).

7 GE-Lunar DXA scanners have a default setting that reports a weight-corrected Z-score. It is recommended that to standardise reporting and maintain consistency between scanners from different manufacturers, this default setting is changed so that Z-scores are reported without weight correction.

8 Before reporting a DXA spine study, careful visual scrutiny of the scan image is essential to exclude artifacts such as degenerative disease, vertebral fractures or metal artifacts that may affect T-score and Z-score values. In elderly subjects the spine scan may be of little value if there is extensive degenerative disease. When reporting a femur study the scan images should be inspected for the correct rotation and abduction of the leg and correct placement of the standard femur regions of interest.

9 When reporting follow-up studies the scan images should be carefully checked to ensure that the positioning of the patient and placement of the regions of interest are consistent. Statistically significant BMD changes require a change of at least 4.5% in spine or total hip BMD.

10 The proposed structure of DXA reporting is as follows:

- The report should begin with the BMD, T- and Z-scores for the spine and femur.
- Where appropriate the use of one of three standardised reports is recommended based on whether the spine and femur T-scores indicate osteoporosis, osteopenia or normal BMD.
- Where necessary the report should end with a free text comment to provide for additional interpretation and recommendations or to qualify the standard reports.

Background

Bone densitometry is now well established in clinical practice and it is generally accepted that DXA is the 'gold standard' technique for the measurement of bone mineral density (BMD). The ability to measure BMD has had a major impact on our ability to diagnose osteoporosis and assist in decisions about treatment. There are countless articles and reviews relating to DXA, but at a practical level there is often confusion among different physicians as to what precisely a DXA result means, and how to apply this to therapeutic decision-making for an individual patient. The purpose of this report is to address these issues and to provide some guidance on standardised reporting of DXA studies. At the present time recommendations will only be made in respect of the spine and the hip.

DXA

Over the past decade, DXA has established itself as the most widely used method of measuring BMD because of its advantages of good precision, short scan times and stable calibration in clinical use. DXA equipment allows scanning of the spine and hip, usually regarded as the most important measurement sites because they are common types of osteoporotic fractures and cause substantial impairment of quality of life, morbidity and mortality. A measurement of hip BMD has been shown to be the most reliable way of evaluating the risk of hip fracture[1,2].

Additionally, since the vertebral bodies are rich in metabolically active trabecular bone, the spine is regarded as the optimum site for monitoring response to treatment[3]. Note that the relationship between bone density and fracture is described by a continuous gradient of risk. Figure 1 shows the relationship between hip bone density and risk of osteoporotic fracture when moving from the highest (I) to the lowest (IV) quartile of BMD[4].

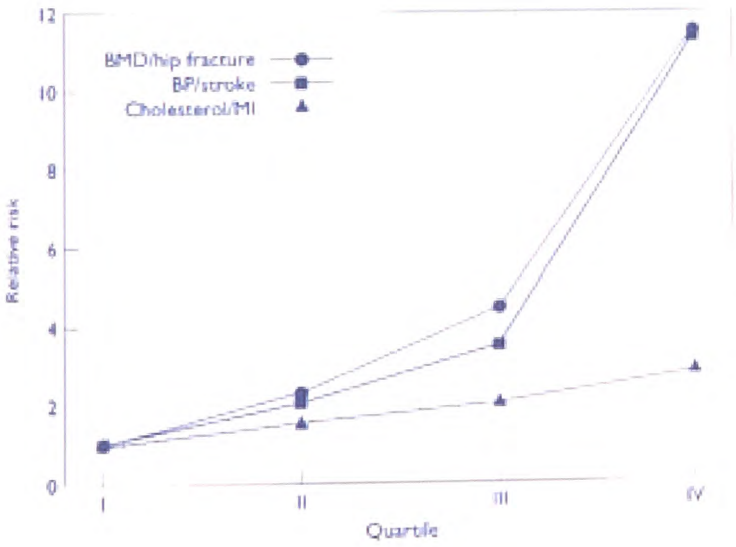


Figure 1. Comparison of the relationship between hip BMD and the risk of hip fracture with the relationships between blood pressure and the risk of stroke and serum cholesterol and the risk of myocardial infarction. In each case the population is divided into quartiles and the relative risk of the higher risk quartiles plotted relative to the lowest risk quartile (figure reproduced from Ref [4] with permission).

The fundamental principle behind DXA is the measurement of the transmission through the body of X-rays of two different photon energies[5]. Since the attenuation coefficient depends on atomic number and photon energy, measurement of the transmission factors at two energies enables the 'areal' densities [i.e. the mass (g) per unit projected area (cm^2)] of two different types of tissue to be inferred. In DXA scans these are taken to be bone mineral (hydroxyapatite) and soft tissue respectively. The radiation dose to the patient from a DXA scan is very low (1 to 10 μSv)[6] and is comparable to the average daily dose from natural background radiation (7 μSv).

Definition of osteoporosis using BMD

In recent years the widespread availability of bone densitometry systems has led to working definitions of osteoporosis that are increasingly based on measurements of bone mineral density (BMD). In particular, in 1994 a World Health Organisation (WHO) study group recommended a definition of osteoporosis based on a BMD measurement of the spine, hip or forearm expressed in standard deviation (SD) units called T-scores[7,8].

The WHO report also proposed a state of reduced BMD intermediate between normal bone density and osteoporosis called osteopenia. It is important to note that these WHO definitions were derived from BMD data from epidemiological studies of Caucasian women in their sixties who had sustained hip fractures, and were never intended as treatment thresholds for individual patients.

The T-score is calculated by taking the difference between a patient's measured BMD and the mean BMD of healthy young adults at the age of peak bone mass, matched for gender and ethnic group, and expressing the difference relative to the young adult population SD:

$$\text{T-score} = \frac{\text{Measured BMD} - \text{Young adult mean BMD}}{\text{Young adult standard deviation}}$$

A T-score result therefore indicates the difference between the patient's BMD and the ideal peak bone mass achieved by a young adult.

The WHO definitions of osteoporosis and osteopenia were originally developed for white females and are based on T-score values such that a woman with a T-score = -2.5 at the spine, hip or forearm is classified as having osteoporosis, a T-score between -2.5 and -1 is classified as osteopenia, while a T-score = -1 is regarded as normal. A fourth state of 'established osteoporosis' was also proposed, denoting osteoporosis as defined above, but in the presence of one or more documented low trauma or fragility fractures, usually of the wrist, spine or hip.

The WHO study group definitions of osteoporosis, osteopenia and normal are intended to identify patients with high, intermediate and low risk of fracture respectively. It is important to recognise that the WHO criteria refer only to BMD measurements of the spine, hip or forearm. These definitions cannot automatically be applied to other BMD measurement sites, to other technologies such as quantitative computed tomography (QCT) or quantitative ultrasound (QUS), or to patients other than caucasian women e.g. men, and to non-caucasians. In particular the use of T-scores is inappropriate in children.

The rationale for the WHO definition of osteoporosis is that it captures around 30% of all Caucasian postmenopausal women[9]. This figure approximates to the lifetime risk of fracture for a 50 year old woman. Furthermore, there is evidence from several recent clinical trials that a T-score of -2.5 is a threshold below which treatment produces a reduction in fracture risk[10,11]. In comparison, it can be argued that the WHO definition of osteopenia captures too high a percentage of women to be clinically useful, and nowadays this term is being used less often, particularly in the context of making therapeutic decisions. In contrast, the WHO definition of osteoporosis has had a major influence on clinical practice, to the extent that the question: 'Does this patient have osteoporosis?' is now regarded as a T-score issue.

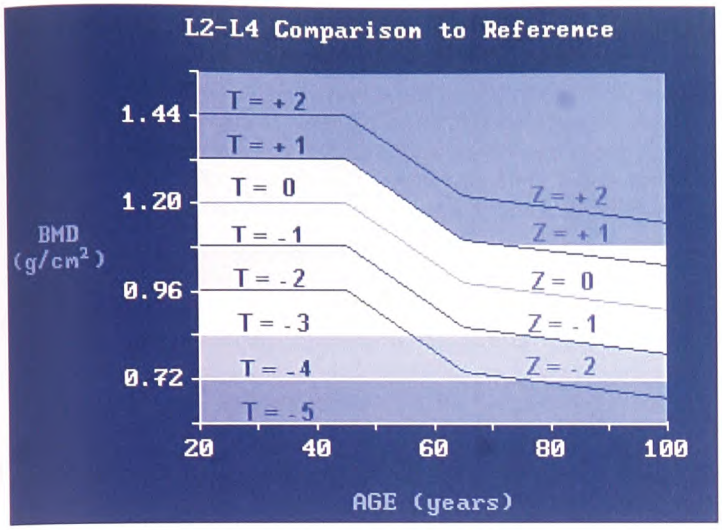
Alongside the T-score, another useful way of expressing BMD measurements is in Z-score units[12]. Like the T-score, the Z-score is expressed in units of the population SD. However, instead of comparing the patient's BMD with the young adult mean, it is compared with the mean BMD expected for the patient's peers, e.g. for a healthy normal subject matched for age, gender and ethnic origin:

$$\text{Z-score} = \frac{\text{Measured BMD} - \text{Aged matched mean BMD}}{\text{Aged matched standard deviation}}$$

GE-Lunar DXA scanners have a default setting that reports a weight-corrected Z-score. It is recommended that to standardise reporting and maintain consistency between scanners from different manufacturers, this default setting is changed so that Z-scores are reported without weight correction. (a)

(a) To turn off the weight correction on GE-Lunar systems click on the Tools menu bar. Then choose Use Options followed by Reference Data. For each site (i.e. spine, femur) make sure that the weight box is clear. If there is a tick in the box, click on the box to remove it. If the scanner is part of a network then this adjustment must be checked on all the scanners in the network.

Figure 2. Caucasian female spine BMD reference data for GE Lunar DXA scanners with lines of constant T-score and Z-score superimposed.



Although not as widely used as T-scores, Z-scores nevertheless remain a useful concept because they express the patient's risk of sustaining an osteoporotic fracture relative to their peers. T- and Z – scores are compared and contrasted in Figure 2 which shows Caucasian female reference data.

Epidemiological studies of the relationship between BMD and fracture incidence are interpreted using a 'gradient of risk' model in which fracture risk increases exponentially with decreasing BMD[13]. The findings are expressed in terms of the relative risk (RR), which is the increase in fracture risk for each 1 SD decrease in BMD. Results for RR values by fracture site and BMD measurement site have been derived in a recent meta-analysis of prospective studies[1]. Typically, every reduction of 1 SD in BMD equates to a 1.5 to 2.5 increase in the likelihood of fracture. It follows therefore that patients with a Z-score < – 1 are at a substantially increased risk of fracture compared to their peers with a Z score of 0.

Reference ranges

If the WHO criterion of a T-score = – 2.5 is used to define osteoporosis, then it is apparent that any errors in the mean BMD or population SD of the reference group might lead to significant differences in the apparent incidence of osteoporosis when applied to other populations. The great majority of centres providing a scanning service use reference ranges provided by the equipment manufacturers, and issues over the accuracy of these ranges have caused controversy in the past, especially for femur BMD[14]. In view of the large number of new devices that are being introduced for the assessment of the skeleton the accuracy of the reference data provided is an important issue.

While there is reasonably close agreement between the principal DXA manufacturers for spine BMD T-scores and Z-scores, for femur reference data the controversy has been largely resolved after a report by the International Committee for Standards in Bone Measurement (ICSBM)[15] which recommended that hip BMD measurements should be interpreted using the total hip region of interest (ROI) (Figure 3) and by employing the hip BMD reference ranges derived from the third US National Health and Nutritional Examination Surveys (NHANES III)[16].

Figure 3. The total hip ROI is shown as the area within this line

The NHANES III survey studied a nationally representative sample of over 14,000 men and women with approximately equal numbers of non-Hispanic white, non-Hispanic black and Mexican Americans. Data were gathered using Hologic QDR 1000 DXA scanners operated from mobile trailers so that subjects from all regions of the United States could be included. The ICSBM report recommended use of the total hip ROI, instead of the previously widely used femoral neck site because of its larger area and therefore improved precision, and the fact that it is the hip region most readily implemented on all manufacturers' systems.

Many centres have already acted upon these recommendations, and the total hip ROI is increasingly being used for scan reporting. It is important to note that these changes affect the percentage of patients who are diagnosed as having osteoporosis at the hip. Using the total hip ROI and the NHANES III reference range, significantly fewer patients will be diagnosed as having osteoporosis than when using the femoral neck ROI and the manufacturer's reference range with Hologic instruments[17]. While it is possible to debate the best choice of measurement site and reference range, it is important to recognize the advantages of a consistent approach, and to have universally accepted DXA BMD criteria for the diagnosis of osteoporosis.

One advantage of presenting bone densitometry results in terms of T- and Z- scores is that they avoid the confusion caused by the raw BMD figures that differ for different manufacturers' equipment[18]. The ICSBM Committee has addressed this latter issue by publishing equations which allow each manufacturer to express their BMD values in a consistent fashion in standardised units (sBMD: units mg/cm^2)[15,19]. The ICSBM report also included figures for the NHANES III total hip reference data converted into sBMD values. It should be noted, however, that sBMD values have not been widely adopted for everyday clinical practice.

Scrutiny of the DXA scan image

Lumbar Spine

A careful visual scrutiny of the scan image is important in the interpretation of DXA studies to ensure that the findings are not affected by anatomical artifacts. For spine scans these include degenerative disease (Figure 4) vertebral fractures (Figure 5) and metal artifacts (Figure 6). Their effect on scan interpretation may be assessed by noting the trend in T- score or Z- score results at each vertebral level.

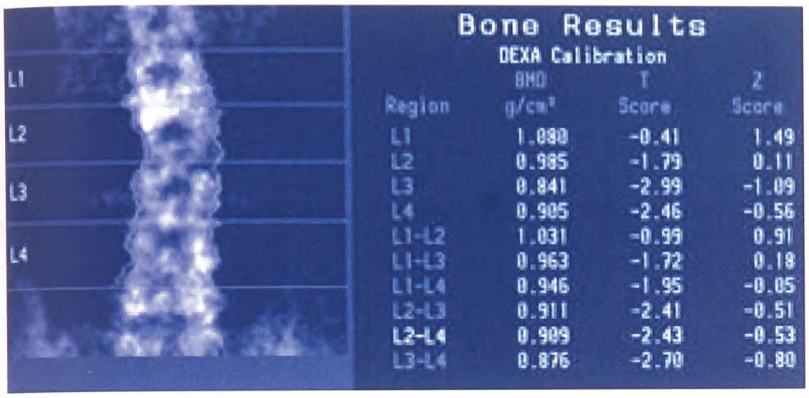


Figure 4. Spine DXA scan from a GE Lunar DPX densitometer showing changes in BMD in L1 and L2 due to osteoarthritis. The effect of OA on BMD can be seen from the trends in T-score and Z-score values from L1 to L4 shown in the first four lines of the BMD report.

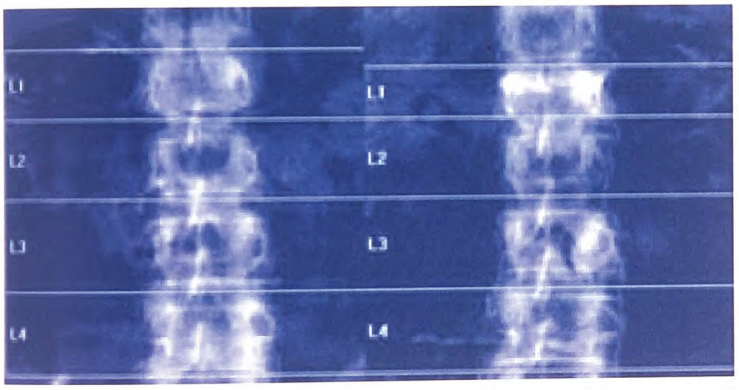


Figure 5. Spine DXA scans from a GE Lunar Expert-XL densitometer showing the development of a vertebral crush fracture in L1 between November 1996 and November 2000

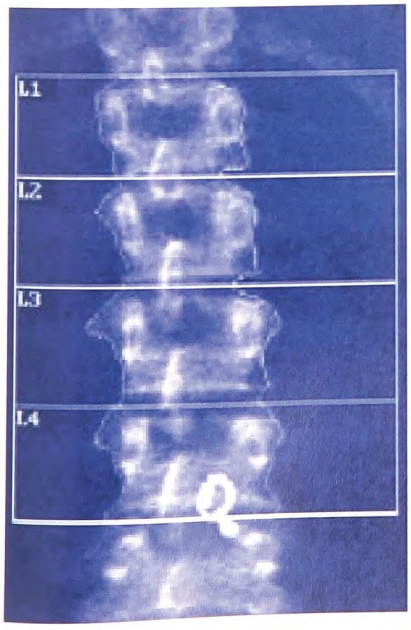


Figure 6. Spine DXA scan from a Hologic QDR4500 densitometer showing the effect on BMD of a gold navel ring superimposed over L4.

If the BMD of an individual vertebra is falsely elevated by an artifact, the affected vertebra(e) should be excluded from analysis and from the reference range plot of BMD against age. If new vertebral fractures are suspected, either by the scan appearance or a change in vertebral height or if there is a large discrepancy in BMD between vertebrae, the referring clinician should be advised about the need for further investigation e.g. with plain radiographs to identify the cause of this difference.

For spine scans it is also important to check that the correct vertebrae have been chosen for analysis. Scan analysis may sometimes be performed by mistake on L1 – L3 or L3 – L5 instead of L2 – L4 [in the case of Lunar machines] and on T12 – L3 or L2 – L5 [in the case of Hologic machines]. Another source of confusion is patients with abnormal segmentation e.g. 6 lumbar vertebrae[20].

In elderly subjects the spine scan may be of little diagnostic value if there is extensive degenerative disease. In such patients a more reliable measure of skeletal status may be obtained from the BMD of the hip and/or a peripheral measurement e.g. forearm or calcaneus.

Proximal Femur

Careful scrutiny of the scan image is also important for femur studies. The hip can show a range of anatomical variants, some of which may make the correct placement of the standard ROI boxes difficult e.g. a short femoral neck, Paget's disease of the femur or exuberant osteoarthritis. Incorrect rotation or abduction of the leg is also a major source of error[21]. Correctly positioned and correctly analysed hip DXA scans are shown in Figure 7 for Hologic and Lunar densitometers respectively. Sometimes optimum hip positioning cannot be obtained even by the most experienced technicians, due to patient limitations e.g. painful osteoarthritis, previous stroke etc.

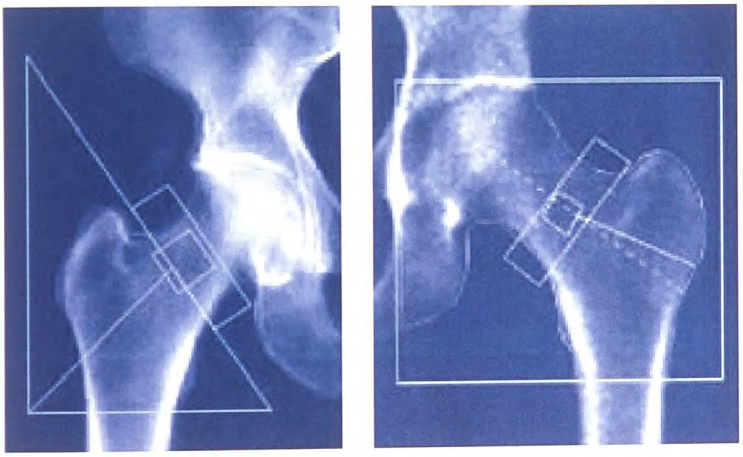


Figure 7. Correctly positioned and correctly analysed femur DXA scans for:
(A) a GE Lunar densitometer; (B) a Hologic QDR densitometer.

Both spine and femur scans need to be checked to ensure that the bone edge markers are correctly positioned. The densitometer algorithms which calculate these are not infallible and manual correction of bone edge markers and intervertebral markers may need to be performed in some cases. The adjacent soft tissue, used in the calculation of the soft tissue baseline, should also be free of artifact. The patient's date of birth must be entered correctly into the densitometer database, since this will affect the calculation of the Z – score.

Inspection of scan images is particularly important when interpreting follow-up studies. A visual comparison should always be made with previous studies. For the spine, a check should be made that the same vertebrae have been used in the analysis. For the femur scan, it is important that the angles of rotation and abduction of the hip are the same and that the ROI boxes have been placed in a consistent manner.

Repeat scans should be performed on the same machine using the same scan mode. The patient's weight also needs to be checked since major weight change can also affect the scan result due to changes in body fat[22]. It is important to remember that a change in software since a previous scan, or a new X-ray tube, may substantially alter the precision of the scanner and add additional variation to the measurements which must be allowed for when calculating 'least significant change' (see below).

A proposed structure fro DXA reporting

The clinical indications for performing BMD measurements are summarized in the Appendix (see page 20). The remainder of this document outlines a scheme for reporting BMD scans of the spine and femur. The basis for scan reporting is the WHO definition of osteoporosis, i.e. a T- score = – 2.5 and this is also the threshold for treatment which has been recommended in the recent RCP Guidelines[23] in the case of postmenopausal women.

The use of T-scores for other patient groups, i.e. premenopausal women, men and children is discussed below. It should be noted that while three standard reports are suggested, any system should have the flexibility to provide individual reports and some of the issues relating to this system will be discussed below.

It is important to begin by reporting BMD, T- and Z- scores:

Spine = ... g/cm2	**T- score =**	**Z- score =**
Femur = ... g/cm2	**T- score =**	**Z- score =**

These figures may then be interpreted with the help of one of three standard reports:

1. **If the T-scores for the spine and total hip BMD are both greater than – 1.0**

   Standard report reads:

   The results are normal and the patient should be reassured.

2. **If at least one T-score for spine or total hip BMD is less than – 1.0 but both are greater than – 2.5**

   Standard report reads:

   The results show osteopenia and treatment may be considered if:

   (a) the patient has previously had a low trauma fracture;

   (b) is receiving glucocorticoid therapy; or

   (c) has a low BMD for age (Z-score of less than -1).

   Even if no treatment is given lifestyle advice to improve BMD should be provided and BMD re-measured in 3 to 5 years.

3. **If at least one T-score for spine or total hip BMD is less than -2.5**

   Standard report reads:

   The results confirm osteoporosis and treatment is indicated

It should be noted that while three standard reports are suggested, any system should have the flexibility to allow for individual reports. A comments box is therefore included to provide for additional reports or to qualify the standard reports.

Additional reporting issues

The reporting suggestions outlined above are intended primarily for post-menopausal women up to the age of 70 or 75 years. They do not cover all situations, and for example are inappropriate for children and pre-menopausal women. Some caution in interpretation is also required when dealing with men or individuals of other races. The rules do not work so well in the elderly, as the majority of individuals over the age of 75 will have osteoporosis based on the WHO definition, while a Z-score of – 1 is too low a threshold in this population. However, in the elderly bone density is often only one of several factors that should be taken into account when making a decision as to whether treatment for osteoporosis is appropriate.

Although there is strong evidence for a reduction in fracture risk with antiresorptive drugs only in patients with vertebral fractures or with a T-score less than -2.5, several authorities (the Royal College of Physicians in the UK, and the National Osteoporosis Foundation in the USA) have proposed that the T-score threshold of -2.5 be raised for patients with a history of low-trauma fractures (23) or in patients receiving corticosteroid therapy[24]. For women over the age of 65 years all those with low bone density for age (Z-score of less than -1) will have a T-score of less than -2.5. However, below the age of 65 years some of these women will have a T-score in the osteopenic range. Because of the strong evidence for a reduction in the rate of bone loss with antiresorptive drugs for patients with osteopenia, some authorities have proposed that women in this latter group should be offered treatment to prevent bone loss. These are the reasons for the special categories included in the osteopenia report above.

Follow-up DXA scans have traditionally been performed to monitor response to anti-resorptive treatment. The appropriate interval between serial BMD scans is determined from the concept of the 'least significant change' in BMD. For any change in BMD to be 'true' with 95% confidence, the measured change must exceed 2.8 (or 2v2) times the precision error (or coefficient of variation) of the measurement[25]. Although the coefficient of variation for PA spine and total hip BMD measurements is often quoted as 1% it is important to realize that this is an idealised figure which applies only to short-term precision measurements (i.e. repeated measurements made over periods of a few hours or days) in young adults with normal BMD and normal weight for height. In practice the relevant figure for precision is the long-term precision error measured over months or years. Patel et al[26] reported long-term precision errors of 1.6% for PA spine and total hip BMD, thereby producing a figure of 4.5% for the least significant change. This figure may be significantly larger, however, in patients with osteoporosis or obesity (i.e. BMI > 30 kg/m^2) and care is therefore required when interpreting BMD changes in such subjects. Since it is unlikely that such a significant change in BMD will be detectable in less than two years, BMD scans are normally not repeated more frequently than every two years.

Referring physicians should be aware that in all cases patients require advice about a healthy well-balanced diet to ensure adequate calcium and vitamin D intake. Other lifestyle issues such as exercise, avoidance of smoking and moderation in alcohol consumption also need to be discussed. In a patient with osteoporosis it is important to exclude potential secondary causes of bone loss such as thyrotoxicosis, primary hyperparathyroidism, hypogonadism especially in males, inflammatory bowel disease, gluten-sensitive enteropathy (which may often be asymptomatic) and myeloma, although such diseases are uncommon.

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Appendix

Referral Criteria for DXA

Clinical indications for BMD measurement are shown in the table below which is reproduced from the Royal College of Physicians guidelines[27]:

Risk Factors providing indications for the diagnostic use of bone densitometry

1. **Presence of strong risk factors**

- **Estrogen deficiency**

  Premature menopause (age < 45 years)
  Prolonged secondary amenorrhoea (>1 year)
  Primary hypogonadism

- **Corticosteroid therapy**

  Prednisolone > 7.5 mg/day for 1 year or more

- **Maternal family history of hip fracture**

- **Low body mass index (< 19 kg/m^2)**

- **Other disorders associated with secondary osteoporosis**

  Anorexia nervosa
  Malabsorption syndrome
  Primary hyperparathyroidism
  Post-transplantation
  Chronic renal failure
  Hyperthyroidism
  Prolonged immobilisation
  Cushing's syndrome

2. **Radiographic evidence of osteopenia and/or vertebral deformity**
3. **Previous fragility fracture, especially of the hip, spine or wrist**
4. **Loss of height, thoracic kyphosis (after radiographic confirmation of vertebral deformities)**

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Guidelines for the provision of a clinical bone densitometry service

National Osteoporosis Society

April 2002

National Osteoporosis Society

Guidelines for the provision of a clinical bone densitometry service

These guidelines are designed to assist practitioners in the development of hospital-based bone densitometry services including axial dual-energy X-ray absorptiometry (DXA), which is the current technique of choice. The guidelines should also be of value to commissioners and service providers when examining the quality of local bone densitometry provision.

The guidelines should be read in conjunction with the following:

- Position statement on the reporting of dual-energy X-ray absorptiometry bone mineral density scans
- Position statement on the use of peripheral dual-energy X-ray absorptiometry in the management of osteoporosis
- Position statement on the use of quantitative ultrasound in the management of osteoporosis

This statement was prepared for the NOS by Ms SA Steel, Dr JD McCrea and Dr PJ Ryan and represents the consensus view of the members of Bone Densitometry Forum. The statement is endorsed by the NOS Council of Management.

April 2002

Key recommendations

1 Requests for bone densitometry scans should only be made by registered medical practitioners, or other relevant health professionals (eg specialist osteoporosis nurse) who are entitled, under their employer's procedures, to refer an individual for a scan. The request should be in writing and with adequate clinical information to enable the appropriateness of the scan to be determined by the scanning centre.

2 Locally agreed evidence-based guidelines for referral and referral forms should be produced and updated regularly by the service commissioners, users and providers.

3 The scanning centre should provide patients with detailed information about osteoporosis and its treatment, access to an osteoporosis nurse specialist or an equivalent health professional for individual discussion, and access by medical referral to a specialist metabolic bone clinic when necessary.

4 Each scanning centre must have prepared full written protocols covering every technical and scientific aspect of its service and these must be read by all staff, regularly updated and be available for inspection at all times.

5 Operators of densitometry equipment should receive adequate training including training in ionising radiation in addition to any training supplied by the manufacturers, their distributors or agents.

6 Scans should be reported promptly by registered medical practitioners with special training in the scientific and technical aspects of bone densitometry as well as clinical training in the diagnosis and management of metabolic bone diseases in general and in osteoporosis in particular.

7 Scan reports should be communicated in writing to the referring practitioner with a medical interpretation of the results and individualised clinical advice on the further management of each patient.

8 All staff participating in densitometry scanning are required to keep their knowledge up to date by participating regularly in appropriate continuing professional development including education and audit.

Procedures and organisation

1 Written guidelines for appropriate referral to the bone densitometry unit should be formulated after discussion with commissioners and medical users of the service. The Royal College of Physicians Guidelines[1] provide nationally accepted and evidence-based referral criteria. Local referral criteria, based on best scientific evidence, should be widely disseminated and regularly reviewed.

2 Scans should only be performed following the receipt of a written request from a medically qualified practitioner indicating the reason for referral. A standard request form, which includes the criteria for referral, should be produced and this should be made available to all medical users of the service. This form should be reviewed and modified at appropriate intervals.

3 Scan requests should be assessed by the medical practitioner(s) responsible for the service. Requests should be graded according to the level of priority; this may be delegated to a suitably qualified health care professional e.g. the densitometer operator, working within designated protocols defined by the medical practitioner responsible for the service who will continue to retain overall responsibility.

4 Any unusual requests or those requiring procedures outside the standard protocols should be discussed with the medical practitioner. Unsuitable requests should be discussed with the referring doctor.

5 A written appointment should be sent to the patient, with an explanation as to the nature and purpose of the test, and directions as to how to reach the scanning centre. The appointment letter should contain information on suitable clothing and provide contact numbers if the patient has any particular requirements or concerns or if the appointment has to be changed.

6 It is suggested that patients receive their appointment letter within two weeks of the scan request being received, with routine scans being performed within three months of receiving the scan request. Procedures should also be in place to be able to perform scans urgently where necessary.

7 A risk factor questionnaire may be used and either completed when the patient attends for the scan or sent to the patient with the appointment letter and discussed on attendance.

8 A diary of appointments should be kept and a daily work schedule should be referred to on each working day. There should be a policy established for non-attenders.

9 Each patient should be welcomed upon arrival by the receptionist and any concerns regarding the scan addressed. Any delays in the scan appointment should be communicated in a timely manner to the patient.

10 A suitable waiting area should be available for patients and their relatives.

11 The scan should be performed in a suitable environment with adequate space, privacy and access to changing facilities. Disabled individuals should have access to suitable facilities (e.g. lifts, toilets) and to nursing care if necessary. Nursing care should also be available to assist with ill patients. A call button should be available for emergencies.

12 Appropriate resuscitation facilities should be available and staff trained to an appropriate level to administer resuscitation, as agreed by the organisation's resuscitation officer and other relevant responsible bodies.

13 Information on osteoporosis should be freely available at the scanning centre together with details of local patient support groups such as those run by the National Osteoporosis Society. Ideally, a nurse counsellor should provide advice on lifestyle measures to promote bone health at the time of referral. Before leaving the scanning centre, every patient should be advised to contact his or her referring doctor to discuss the results.

14 Scans should be reported promptly by a medical practitioner who is proficient in the field of osteoporosis and bone densitometry. The result should also be sent promptly to the referring doctor and should normally include both a medical interpretation of the results and either appropriate advice or reference to locally agreed treatment and/or management guidelines. Ideally, scan results should be issued within seven to ten days.

15 In addition to the bone density scan, referring doctors should also have the option of sending patients to an osteoporosis or metabolic bone clinic for further advice and assessment if this is considered necessary for patient management.

Protocols and equipment

1 Local written procedures covering all aspects of the bone densitometry service should be available in the scanning centre and read by all involved in bone densitometry. These must be kept in a recognised location and regularly updated. This is now a legal requirement following the introduction of the new Ionising Radiation Regulations[2] and the Ionising Radiations (Medical Exposure) Regulations[3].

2 There should be a written procedure regarding women of childbearing age. DXA scans of appropriate sites e.g. forearm or heel, should only be performed in pregnant women with the explicit approval of the medical practitioner with overall responsibility for the service.

3 Written quality control procedures must be established and adhered to, usually as specified by the manufacturer.

4 An adequate database of the service should be kept to enable review of studies and audit to be performed. Such audits are to be recommended following the introduction of Clinical Governance[4]. The provisions of the Data Protection Act[5] should be adhered to.

5 Scan acquisition and analysis should be performed by trained operators and should be conducted according to standardised protocols based on the manufacturer's guidelines. Optimum results are obtained by the deployment of a small number of dedicated operators.

6 Before sending scans for clinical reporting, they should be reviewed at the DXA computer workstation to ensure that the data have been acquired and processed accurately, that artefacts have been identified correctly and to facilitate reprocessing if this is necessary.

7 Results should be both archived and backed-up onto suitable digital media. A hard copy should also be retained.

8 Written maintenance procedures should be agreed and a maintenance contract established with an appropriately trained individual or company, usually the national distributor or the manufacturer. Service and repair records must be kept, including details of any faults discovered, and these must be available for inspection at any time.

9 The importance of equipment safety should be recognised. Equipment must be operated according to national and local standards for radiation protection, electrical safety, fire regulations and in accordance with health and safety legislation. Written evidence of compliance with these standards should be kept within the department. The Radiation Protection Advisor (RPA) must approve the site where scanning occurs and the Radiation Protection Supervisor (RPS) must ensure compliance with Local Rules regarding radiation safety[2,6].

10 The choice and commissioning of new equipment should be made with expert help and advice from suitably qualified individuals e.g. clinical scientist and clinician.

Staffing

Operators

1 Operators should be adequately trained health care professionals, generally radiographers, nurses or clinical technologists. They should expect to receive equipment specific training by the company supplying the scanner. Further training is usually required and they should be encouraged to attend courses such as those organised by the National Osteoporosis Society or the International Society for Clinical Densitometry (ISCD). Operators must continue to maintain their skills and knowledge.

2 The Ionising Radiations (Medical Exposure) Regulations[3] state that ' ... no practitioner or operator shall carry out a medical exposure ... without having been adequately trained.' This means that ' ... practitioners and operators shall have successfully completed training, including theoretical knowledge and practical experience in ... radiation production, radiation protection and statutory obligations relating to ionising radiation.'

3 Operators must have a sufficient grounding in the field of osteoporosis to be able to explain the purpose and nature of the test to the patient. Operators must also be familiar with the importance of good positioning and be able to acquire, analyse and archive studies in accordance with the manufacturer's guidance and local procedures. They must also be able to recognise artefacts, be able to perform routine quality assurance with a suitable phantom prior to scanning patients and be aware of procedures to be followed when devices are not working correctly.

Scientific support

4 To ensure continued good quality control and performance, a suitably qualified medical physics expert should be involved as appropriate. The Ionising Radiations (Medical Exposure) Regulations[3] state that in respect of a medical physicist the requirement is for ' ... a person who holds a science degree ... and is experienced in the application of physics to the diagnostic uses of ionising radiation.'

5 There must be a clearly identifiable scientist responsible, whose duties will include the supervision and analysis of quality control data, troubleshooting of faults, training of operators and advice on radiation protection. The medical physics expert should demonstrate continued professional competence through membership of a recognised professional body. Professional membership of the National Osteoporosis Society is also recommended.

Clinician

6 Medical practitioners should have clinical responsibility for the service and be suitably proficient in the field of bone densitometry and osteoporosis. They should be able to demonstrate adequate training and where specified, have complied with Royal College requirements. Training would generally be expected to take place in a bone specialist unit with densitometry.

7 They should define a protocol for validation and prioritisation of densitometry requests. They should assist with the development of local protocols particularly relating to sites to be measured. Clinicians should be familiar with the basic principles of DXA and the operation of their own equipment including precision. They should be responsible for the issuing of reports as detailed above.

8 They must be familiar with the clinical utility of the test and the importance and clinical relevance of T-scores, Z-scores, the WHO definitions and risk assessment[7]. They must be able to recognise anomalies, artefacts and confounding pathology. When reporting repeat bone density scans, they must make allowance for factors such as expected annual change and precision in assessing the net percent change in bone density over time. Similarly, they should recommend repeat scans only at intervals at which significant clinical change is likely to be demonstrated.

9 They must be able to demonstrate that they participate in continuing medical education relevant to the running of a bone densitometry service. It is recommended that they retain professional membership of an appropriate organisation such as the National Osteoporosis Society.

Administrative and Clerical

10 Sufficient administrative and clerical support should be available for the efficient booking of scans, sending out of appointments, typing of results and sending these to referring clinicians.

11 Ideally, a designated receptionist should be available to welcome patients and help with practical arrangements.

Nursing

12 Trained nursing support will be required if services are scanning sick individuals.

Radiation protection advice

13 The RPA must approve the premises and local procedures. The RPS should be identified and should take responsibility for ensuring adherence to Local Rules[6].

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